

02-05-2010

10/598,789A Yong Chu ~~07-08-2008~~

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TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

NEWS 1 Web Page for STN Seminar Schedule - N. America
NEWS 2 JAN 02 STN pricing information for 2008 now available
NEWS 3 JAN 16 CAS patent coverage enhanced to include exemplified
prophetic substances
NEWS 4 JAN 28 USPATFULL, USPAT2, and USPATOLD enhanced with new
custom IPC display formats
NEWS 5 JAN 28 MARPAT searching enhanced
NEWS 6 JAN 28 USGENE now provides USPTO sequence data within 3 days
of publication
NEWS 7 JAN 28 TOXCENTER enhanced with reloaded MEDLINE segment
NEWS 8 JAN 28 MEDLINE and LMEEDLINE reloaded with enhancements
NEWS 9 FEB 08 STN Express, Version 8.3, now available
NEWS 10 FEB 20 PCI now available as a replacement to DPCI
NEWS 11 FEB 25 IFIREF reloaded with enhancements
NEWS 12 FEB 25 IMSPRODUCT reloaded with enhancements
NEWS 13 FEB 29 WPINDEX/WPIDS/WPIX enhanced with ECLA and current
U.S. National Patent Classification
NEWS 14 MAR 31 IFICDB, IFIPAT, and IFIUDB enhanced with new custom
IPC display formats
NEWS 15 MAR 31 CAS REGISTRY enhanced with additional experimental
spectra
NEWS 16 MAR 31 CA/CAPLUS and CASREACT patent number format for U.S.
applications updated
NEWS 17 MAR 31 LPCI now available as a replacement to LDPCI
NEWS 18 MAR 31 EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 19 APR 04 STN AnaVist, Version 1, to be discontinued
NEWS 20 APR 15 WPIDS, WPINDEX, and WPIX enhanced with new
predefined hit display formats
NEWS 21 APR 28 EMBASE Controlled Term thesaurus enhanced
NEWS 22 APR 28 IMSRESEARCH reloaded with enhancements
NEWS 23 MAY 30 INPAFAMDB now available on STN for patent family
searching
NEWS 24 MAY 30 DGENE, PCTGEN, and USGENE enhanced with new homology
sequence search option
NEWS 25 JUN 06 EFFULL enhanced with 260,000 English abstracts
NEWS 26 JUN 06 KOREAPAT updated with 41,000 documents
NEWS 27 JUN 13 USPATFULL and USPAT2 updated with 11-character
patent numbers for U.S. applications
NEWS 28 JUN 19 CAS REGISTRY includes selected substances from
web-based collections
NEWS 29 JUN 25 CA/CAPLUS and USPAT databases updated with IPC
reclassification data
NEWS 30 JUN 30 AEROSPACE enhanced with more than 1 million U.S.

NEWS 31 JUN 30 patent records
 EMBASE, EMBAL, and LEMBASE updated with additional
 options to display authors and affiliated
 organizations
 NEWS 32 JUN 30 STN on the Web enhanced with new STN AnaVist
 Assistant and BLAST plug-in
 NEWS 33 JUN 30 STN AnaVist enhanced with database content from EPFULL
 NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
 AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.
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***** STN Columbus *****

FILE 'HOME' ENTERED AT 21:14:57 ON 08 JUL 2008

=> file reg
 COST IN U.S. DOLLARS SINCE FILE TOTAL
 ENTRY SESSION
 FULL ESTIMATED COST 0.21 0.21

FILE 'REGISTRY' ENTERED AT 21:15:19 ON 08 JUL 2008
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Property values tagged with IC are from the ZIC/VINITI data file
 provided by InfoChem.

STRUCTURE FILE UPDATES: 7 JUL 2008 HIGHEST RN 1032964-85-4
 DICTIONARY FILE UPDATES: 7 JUL 2008 HIGHEST RN 1032964-85-4

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

Please note that search-term pricing does apply when
 conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
 predicted properties as well as tags indicating availability of
 experimental property data in the original document. For information
 on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

=>
 Uploading C:\Documents and Settings\ychu\Desktop\Case\10598789\10598789A.str



```

chain nodes :
10 11 13 14 16
ring nodes :
1 2 3 4 5 6 7 8 9 17 18 19 20 21 22 23 24 25
chain bonds :
8-10 9-13 10-11 10-17 14-16
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 17-18 17-21 18-19 19-20 20-21
20-22 21-25 22-23 23-24 24-25
exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 9-13 10-11 10-17 14-16 17-18
17-21 18-19 19-20 20-21 20-22 21-25 22-23 23-24 24-25
exact bonds :
8-10

```

G2:H,CH,t-Bu

```

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom 22:Atom
23:Atom 24:Atom 25:Atom

```

L1 STRUCTURE UPLOADED

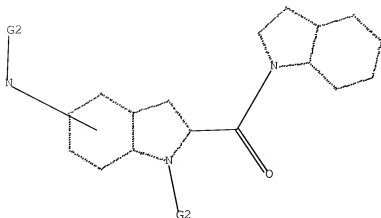
=> d

L1 HAS NO ANSWERS

L1 STR

full scope

Group II with claim 2



G1
G2 H, CH, t-Bu

Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 21:16:01 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 511 TO ITERATE

100.0% PROCESSED 511 ITERATIONS
SEARCH TIME: 00.00.01

22 ANSWERS

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 8864 TO 11576
PROJECTED ANSWERS: 159 TO 721

L2 22 SEA SSS SAM L1

=> d dscan

'DSCAN' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'

The following are valid formats:

Substance information can be displayed by requesting individual fields or predefined formats. The predefined substance formats are: (RN = CAS Registry Number)

REG - RN
SAM - Index Name, MF, and structure - no RN
FIDE - All substance data, except sequence data
IDE - FIDE, but only 50 names
SQIDE - IDE, plus sequence data
SQIDE3 - Same as SQIDE, but 3-letter amino acid codes are used
SQD - Protein sequence data, includes RN
SQD3 - Same as SQD, but 3-letter amino acid codes are used
SQN - Protein sequence name information, includes RN

EPROP - Table of experimental properties
PPROP - Table of predicted properties

PROP - EPROP, ETAG, PPROP and SPEC

Any CA File format may be combined with any substance format to obtain CA references citing the substance. The substance formats must be cited first. The CA File predefined formats are:

ABS -- Abstract
APPS -- Application and Priority Information
BIB -- CA Accession Number, plus Bibliographic Data
CAN -- CA Accession Number
CBIB -- CA Accession Number, plus Bibliographic Data (compressed)
IND -- Index Data
IPC -- International Patent Classification
PATS -- PI, SO
STD -- BIB, IPC, and NCL

IABS -- ABS, indented, with text labels
IBIB -- BIB, indented, with text labels
ISTD -- STD format, indented

OBIB ----- AN, plus Bibliographic Data (original)
OIBIB ----- OBIB, indented with text labels

SBIB ----- BIB, no citations
SIBIB ----- IBIB, no citations

The ALL format gives FIDE BIB ABS IND RE, plus sequence data when it is available.

The MAX format is the same as ALL.

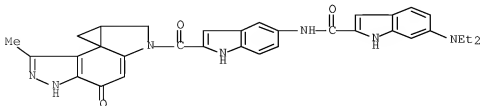
The IALL format is the same as ALL with BIB ABS and IND indented, with text labels.

For additional information, please consult the following help messages:

HELP DFIELDS -- To see a complete list of individual display fields.
HELP FORMATS -- To see detailed descriptions of the predefined formats.
ENTER DISPLAY FORMAT (IDE):end

=> d scan

L2 22 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN 1H-Indole-2-carboxamide, 6-(diethylamino)-N-[2-[(4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[3,4]pyrrolo[3,2-e]indazol-2(1H)-yl)carbonyl]-1H-indol-5-yl]-
MF C33 H31 N7 O3
CI COM

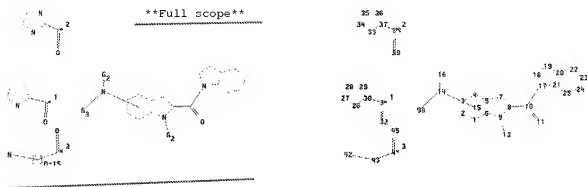


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=>

Uploading C:\Documents and Settings\ychu\Desktop\Case\10598789\10598789B.str



```

chain nodes :
10 11 13 14 16 31 32 38 39 42 43 44 45 50
ring nodes :
1 2 3 4 5 6 7 8 9 17 18 19 20 21 22 23 24 25 26 27 28 29 30
33 34 35 36 37
chain bonds :
8-10 9-13 10-11 10-17 14-16 14-50 30-31 31-32 37-38 38-39 42-43 43-44
44-45
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 17-18 17-21 18-19 19-20 20-21
20-22 21-25 22-23 23-24 24-25 26-27 26-30 27-28 28-29 29-30 33-34 33-37
34-35 35-36
36-37
exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 9-13 10-11 10-17 14-16 14-50
17-18 17-21 18-19 19-20 20-21 20-22 21-25 22-23 23-24 24-25 26-27 26-30
27-28 28-29
29-30 31-32 33-34 33-37 34-35 35-36 36-37 38-39 42-43 44-45
exact bonds :
8-10 30-31 37-38 43-44

```

G2:H,CH,t-Bu

G3:[*1],[*2],[*3]

Match level :

```

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom 22:Atom
23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 31:CLASS
32:CLASS 33:Atom
34:Atom 35:Atom 36:Atom 37:Atom 38:CLASS 39:CLASS 42:CLASS 43:CLASS
44:CLASS 45:CLASS
50:CLASS

```

L3 STRUCTURE UPLOADED

=> d

L3 HAS NO ANSWERS

L3 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s l3

SAMPLE SEARCH INITIATED 21:24:39 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 354 TO ITERATE

100.0% PROCESSED 354 ITERATIONS

13 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

 BATCH **COMPLETE**

PROJECTED ITERATIONS: 5952 TO 8208

PROJECTED ANSWERS: 44 TO 476

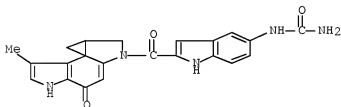
L4 13 SEA SSS SAM L3

=> d scan

L4 13 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN

IN Cyclopropa[c]pyrrolo[3,2-e]indol-4(5H)-one, 2-[[5-[(aminocarbonyl)amino]-1H-indol-2-yl]carbonyl]-1,2,8a-tetrahydro-7-methyl- (9CI)

MF C22 H19 N5 O3



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

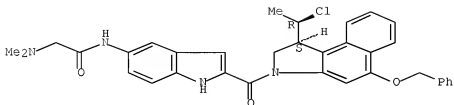
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L4 13 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN

IN Acetamide, N-[2-[[[(1S)-1-[(1R)-1-chloroethyl]-1,2-dihydro-5-(phenylmethoxy)-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-2-

(dimethylamino)-
MF C34 H33 Cl N4 O3

Absolute stereochemistry. Rotation (+).

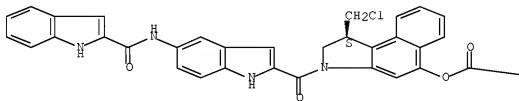


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 13 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Carbamic acid, dimethyl-, (1S)-1-(chloromethyl)-2,3-dihydro-3-[[5-[(1H-indol-2-ylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-1H-benz[e]indol-5-yl ester (9Cl)
MF C34 H28 Cl N5 O4

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 1-B

—NMe2

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

~~=> s l13 full~~
~~L5 13 LL3~~

=> s l3 full

FULL SEARCH INITIATED 21:25:56 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 7282 TO ITERATE

100.0% PROCESSED 7282 ITERATIONS 343 ANSWERS
SEARCH TIME: 00.00.01

L6 343 SEA SSS FUL L3

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	191.33	191.54

FILE 'CAPLUS' ENTERED AT 21:26:04 ON 08 JUL 2008
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FILE COVERS 1907 - 8 Jul 2008 VOL 149 ISS 2
FILE LAST UPDATED: 7 Jul 2008 (20080707/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2008.

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/legal/infopolicy.html>

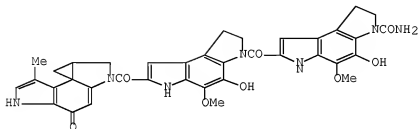
=> s l6

L7 183 L6 **Too many references**

=> d ibib abs hitstr 175-183

L7 ANSWER 175 OF 183 CAPLUS COPYRIGHT 2008 ACS ON STN
ACCESSION NUMBER: 1988:124054 CAPLUS Full-text
DOCUMENT NUMBER: 108:124054
ORIGINAL REFERENCE NO.: 108:20145a,20148a
TITLE: Mutagenicity of the antitumor antibiotic CC-1065 and its analogs in mammalian (V79) cells and bacteria
AUTHOR(S): Harbach, Philip R.; Zimmer, David M.; Mazurek, John H.; Bhuyan, Bijoy K.
CORPORATE SOURCE: Dep. Pathol. Toxicol. Res., Upjohn Co., Kalamazoo, MI,

SOURCE: 49001, USA
Cancer Research (1988), 48(1), 32-6
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

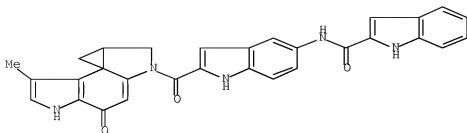
AB The mutagenicity for V79 cells (6-thioguanine resistance) and Salmonella (histidine auxotrophy or azaguanine resistance) of selected analogs of CC-1065 (I) was compared to DNA-binding activity and the structure-activity relationship was detd. CC-1065, U-62,736, U-66,866, U-66,694, U-67,786, and U-68,415 all have an A segment with an intact cyclopropyl group and different B segments. The cyclopropyl group is absent from U-66,226 and U-63,360. Elimination of the cyclopropyl ring diminished the cytotoxic and mutagenic potency of the compds. such that U-63,360 was nearly 3 orders of magnitude less potent than CC-1065 in V79 cells. For the compds. with an intact cyclopropyl group, the order of cytotoxic and mutagenic potency (molar basis) in V79 cells generally correlated with binding to calf thymus DNA, and increased with the length of the B segment. Thus, the order of cytotoxicity was CC-1065 > U-68,415 > U-66,694 > U-66,866 > U-62,736. U-67,786 cell outside this pattern since it was more cytotoxic and mutagenic than U-66,694, although it was of a similar size and had similar DNA-binding activity. These results show that an electrophilic C afforded by an intact cyclopropyl group of this type is necessary but not sufficient to account for the high cytotoxic and mutagenic potency of CC-1065 and U-68,415. The size and characteristics of the B segment also affect the potency. At an equitoxic (10 or 50% LD) dose, an inverse relationship exists between cytotoxic and mutagenic potency such that at the 50% LD, the least cytotoxic compd. (U-62,736) was more mutagenic than the most cytotoxic compd. (CC-1065). Apparently, the more cytotoxic analogs are less mutagenic (at an equitoxic dose) because they may have greater structure-directed binding to less mutable DNA sites in the minor groove.

IT 104713-40-8

RL: BIOL (Biological study)
(cytotoxic and mutagenic activities of, DNA binding in, structure in relation to)

RN 104713-40-8 CAPLUS

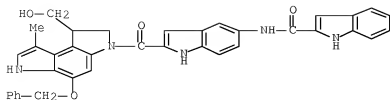
CN 1H-Indole-2-carboxamide, N-[2-[(4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl)carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)



L7 ANSWER 176 OF 183 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 1988:94431 CAPLUS Full-text
 DOCUMENT NUMBER: 108:94431
 ORIGINAL REFERENCE NO.: 108:15531a,15534a
 TITLE: Stereoelectronic factors influencing the biological activity and DNA interaction of synthetic antitumor agents modeled on CC-1065
 AUTHOR(S): Warpehoski, M. A.; Gebhard, I.; Kelly, R. C.; Krueger, W. C.; Li, L. H.; McGovren, J. P.; Prairie, M. D.; Wicniewski, N.; Wierenga, W.
 CORPORATE SOURCE: Res. Lab., Upjohn Co., Kalamazoo, MI, 49001, USA
 SOURCE: Journal of Medicinal Chemistry (1988), 31(3), 590-603
 CODEN: JMCMAR; ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 108:94431
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The synthesis, physicochem. properties, and biol. activities of 21 novel spiro cyclopropyl compds., e.g. I [R = H, SO₂Ph, CO₂Me₃, COMe, substituted (indol-2-yl)carbonyl], prepd. by intramol. cyclopropanation of pyrroloindoles II (R₁ = PhCH₂, R₂ = SO₂CF₃; R₁ = R₂ = H), are described. Many I are more effective than the antitumor antibiotic CC-1065 (III) against murine tumors. In particular, IV exhibits high activity and potency. Structure-activity anal. supports a mol. mechanism of biol. action involving hydrophobic interaction of the drug with DNA and acid-catalyzed alkylation of DNA.
 IT 101134-50-3P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (prepn. and mesylation of)
 RN 101134-50-3 CAPLUS
 CN 1H-Indole-2-carboxamide, N-[2-[[1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

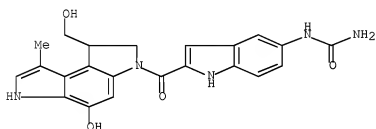


IT 112090-00-3P 112090-01-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 112090-00-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol, 3-[[5-[(aminocarbonyl)amino]-1H-indol-2-yl]carbonyl]-1,2,3,6-tetrahydro-5-hydroxy-8-methyl- (9CI) (CA INDEX NAME)



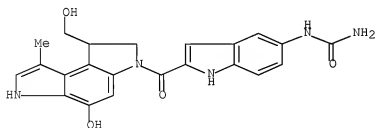
RN 112090-01-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol, 3-[[5-[(aminocarbonyl)amino]-1H-indol-2-yl]carbonyl]-1,2,3,6-tetrahydro-5-hydroxy-8-methyl-, monomethyl ether (9CI) (CA INDEX NAME)

CM 1

CRN 112090-00-3

CMF C22 H21 N5 O4



CM 2

CRN 67-56-1
CMF C H4 O

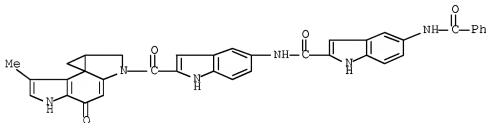
H3C—OH

IT 101134-80-9P 101151-46-6P 101151-47-7E
101713-40-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., antitumor activity, induced CD, and kinetics of ring cleavage
of)

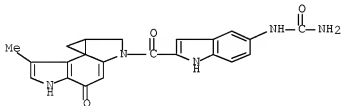
RN 101134-80-9 CAPLUS

CN 1H-Indole-2-carboxamide, 5-(benzoylamino)-N-[2-[(4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl)carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)



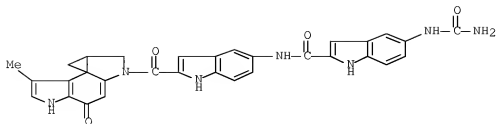
RN 101151-46-6 CAPLUS

CN Cyclopropa[c]pyrrolo[3,2-e]indol-4(5H)-one, 2-[[5-[(aminocarbonyl)amino]-1H-indol-2-yl]carbonyl]-1,2,8,8a-tetrahydro-7-methyl- (9CI) (CA INDEX NAME)



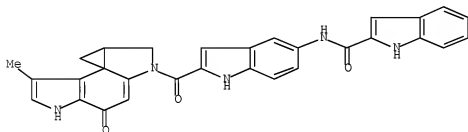
RN 101151-47-7 CAPLUS

CN 1H-Indole-2-carboxamide, 5-[(aminocarbonyl)amino]-N-[2-[(4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl)carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)



RN 104713-40-8 CAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[(4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl)carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)



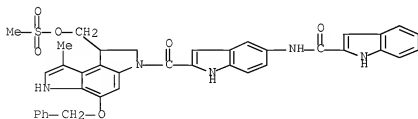
IT 101134-61-6P 101134-62-7P 101134-63-8P

101134-65-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn., debenzoylation, and intramol. cyclopropanation of)

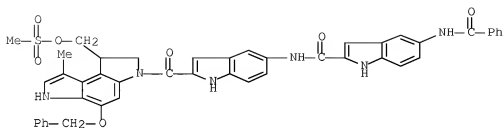
RN 101134-61-6 CAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[[1,6-dihydro-8-methyl-1-[(methylsulfonyl)oxy]methyl]-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



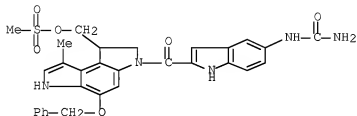
RN 101134-62-7 CAPLUS

CN 1H-Indole-2-carboxamide, 5-(benzoylamino)-N-[2-[[1,6-dihydro-8-methyl-1-[(methylsulfonyl)oxy]methyl]-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



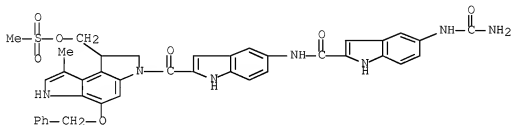
RN 101134-63-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol, 3-[[5-[(aminocarbonyl)amino]-1H-indol-2-yl]carbonyl]-1,2,3,6-tetrahydro-8-methyl-5-(phenylmethoxy)-, methanesulfonate (ester) (9CI) (CA INDEX NAME)



RN 101134-65-0 CAPLUS

CN 1H-Indole-2-carboxamide, 5-[(aminocarbonyl)amino]-N-[2-[[1,6-dihydro-8-methyl-1-[[[(methylsulfonyl)oxy]methyl]-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



L7 ANSWER 177 OF 183 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1988:87686 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 108:87686

ORIGINAL REFERENCE NO.: 108:14287a, 14290a

TITLE: Effects of U-71,184 and several other CC-1065 analogs on cell survival and cell cycle of Chinese hamster ovary cells

AUTHOR(S): Adams, Earl G.; Badiner, Gloria J.; Bhuyan, Bijoy K.
 CORPORATE SOURCE: Upjohn Co., Kalamazoo, MI, 49001, USA
 SOURCE: Cancer Research (1988), 48(1), 109-16
 CODEN: CNREA8; ISSN: 0008-5472
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The effects of several analogs of CC-1065 on inhibition of CHO cell survival, cell progression, and their phase-specific toxicity are reported. CC-1065, U-66,664, U-66,819, U-66,694, and U-71,184 all have a left hand segment with an intact cyclopropyl group but have different tail segments. Lethality of these compds. after 2 h drug exposure was in the following order (50% lethal concn. in nM in parentheses): CC-1065 (0.06) > U-71,184 (1.3) > U-66,694 (3.2) > U-68,819 (171) > U-66,664 (>1200). In general, these compds. did not inhibit progression from G1 to S but slowed progression through S and blocked cells in G2-M. The phase-specific toxicity of U-71,184 and U-66,694 was different from that of CC-1065. CC-1065 was most cytotoxic to cells in M and early G1 and toxicity decreased as cells entered late G1 and S. In contrast, U-66,694 and U-71,184 were most toxic to cells in late G1. The biochem. and cellular effects of U-71,184 were then studied in detail since it was the most active among these analogs. After a 2-h exposure to 3 ng/mL U-71,184, 90% cell kill or growth inhibition was obsd., whereas 100 ng/mL was needed for similar inhibition of DNA and RNA synthesis. This discrepancy between the doses suggested that inhibition of nucleic acid synthesis may not be causally related to lethality. Further studies showed that when drug was removed after 2 h exposure, DNA synthesis continued to be inhibited, whereas RNA and protein synthesis reached levels higher than the control. Therefore, it is likely that at cytotoxic doses the low level of inhibition of DNA synthesis combined with the stimulation of RNA and protein synthesis leads to unbalanced growth and cell death.

IT 104713-39-5, U-71185

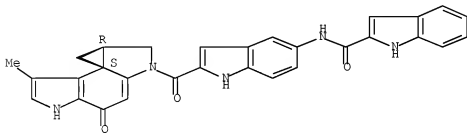
RL: PRP (Properties)

(cytotoxicity of, cell cycle in relation to)

RN 104713-39-5 CAPLUS

CN 1H-indole-2-carboxamide, N-[2-[[[7bS,8aR)-4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa(c)pyrrolo[3,2-e]indol-2(1H)-yl]carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L7 ANSWER 178 OF 183 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1987:597901 CAPLUS Full-text

DOCUMENT NUMBER: 107:197901

ORIGINAL REFERENCE NO.: 107:31735a,31738a

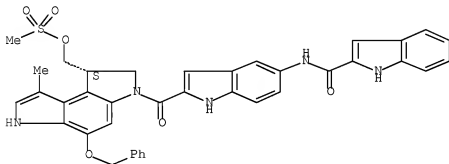
TITLE: Coupling of cyclopropapyrroloindole (CPI) derivatives.
 The preparation of CC-1065, ent-CC-1065, and analogs

AUTHOR(S): Kelly, Robert C.; Gebhard, Ilse; Wicnienski, Nancy;
Aristoff, Paul A.; Johnson, Paul D.; Martin, David G.
CORPORATE SOURCE: Cancer and Viral Dis. Res., Upjohn Co., Kalamazoo, MI,
49001, USA
SOURCE: Journal of the American Chemical Society (1987),
109(22), 6837-8
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 107:197901
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

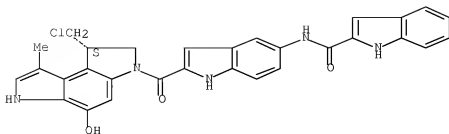
AB CC-1065 (I, R = R1) and its analogs I (R = pentyl, 2-indolyl, R2, X = NH, O)
were prepd. from the pyrroloindole II (R3 = OH, R4 = H, R5 = CH2Ph) via II (R3
= Cl, R4 = CO2Me3, R5 = H), II (R3 = Cl, R4 = R5 = H), and II (R3 = Cl, R4 =
COR, R5 = H). Ent-CC-1065 was similarly prepd. and had an ED50 against
leukemia L1210 of 4.5 .times. 10-12 g/mL.
IT 108833-15-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. and chlorination of)
RN 108833-15-4 CAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[1,6-dihydro-8-methyl-1-
[[(methylsulfonyl)oxy]methyl]-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-
3(2H)-yl]carbonyl]-1H-indol-5-yl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 110314-46-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. and cyclopropanation of)
RN 110314-46-0 CAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,6-dihydro-5-hydroxy-8-
methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]-, (S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 110314-44-8P

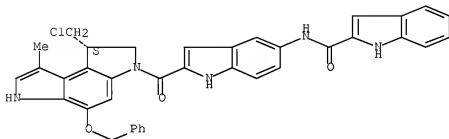
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and hydrogenolysis of)

RN 110314-44-8 CAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,6-dihydro-8-methyl-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



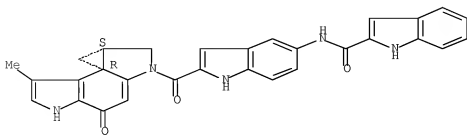
IT 101222-80-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

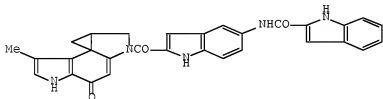
RN 101222-80-4 CAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[[1-(7bR,8aS)-4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl]carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



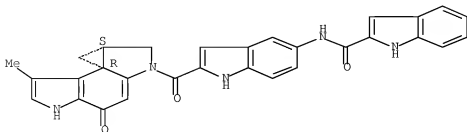
L7 ANSWER 179 OF 183 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 1987:423139 CAPLUS Full-text
 DOCUMENT NUMBER: 107:23139
 ORIGINAL REFERENCE NO.: 107:3903a,3906a
 TITLE: Total synthesis of U-71184, a potent new antitumor agent modeled on CC-1065
 AUTHOR(S): Warpehoski, M. A.
 CORPORATE SOURCE: Upjohn Co., Kalamazoo, MI, 49001, USA
 SOURCE: Tetrahedron Letters (1986), 27(35), 4103-6
 CODEN: TELEAY; ISSN: 0040-4039
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 107:23139
 GI



I

AB U-71184 (I), a highly potent analog of novel antitumor antibiotic CC-1065, involves the unmasking of a p-hydroxyphenethyl mesylate, which undergoes facile intramol. elimination to afford the reactive cyclopropylspirocyclohexadienone. Its enantiomer, U-71185, was also prepd. I had antitumor activity comparable to that of CC-1065 without the delayed toxicity, but U-71185 was inactive.
 IT 101222-80-4P, U-71184 104713-39-5P, U-71185
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (prepn. and antitumor activity of)
 RN 101222-80-4 CAPLUS
 CN 1H-Indole-2-carboxamide, N-[2-[[[(7bR,8aS)-4,5,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl]carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)

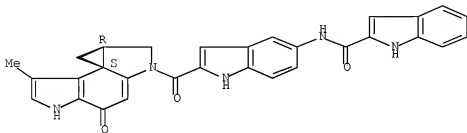
Absolute stereochemistry. Rotation (+).



RN 104713-39-5 CAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[[(7bS, 8aR)-4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl]carbonyl]-1H-indol-5-yl]-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



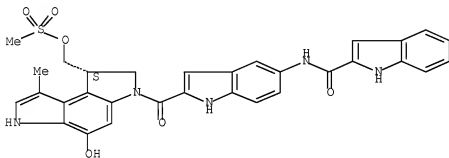
IT 108833-16-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. and cyclopropanation of)

RN 108833-16-5 CAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[[1,6-dihydro-5-hydroxy-8-methyl-1-
[[(methylsulfonyl)oxy]methyl]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-
yl]carbonyl]-1H-indol-5-yl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



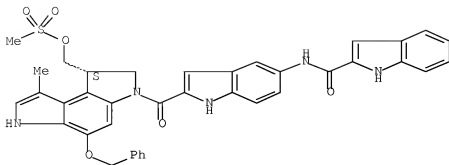
IT 106633-15-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. and debenzoylation of)

RN 108833-15-4 CAPLUS

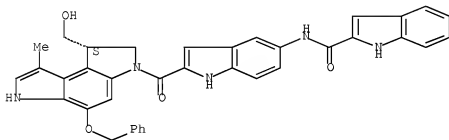
CN 1H-Indole-2-carboxamide, N-[2-[[1,6-dihydro-8-methyl-1-
[[(methylsulfonyl)oxy]methyl]-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-
3(2H)-yl]carbonyl]-1H-indol-5-yl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

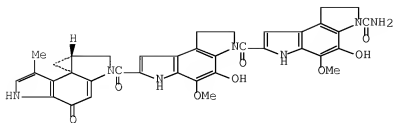


IT 108859-64-9P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (prepn. and mesylation of)
 RN 108859-64-9 CAPLUS
 CN 1H-Indole-2-carboxamide, N-[2-[[1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-
 (phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-
 yl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 180 OF 183 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 1987:12465 CAPLUS [Full-text](#)
 DOCUMENT NUMBER: 106:12465
 ORIGINAL REFERENCE NO.: 106:2037a,2040a
 TITLE: L1210 cell growth inhibition, DNA synthesis
 inhibition, and DNA binding properties of CC-1065
 analogs
 AUTHOR(S): Krueger, W. C.; Prairie, M. D.; Wallace, T. L.;
 Moscovitz, A.; Li, L. H.
 CORPORATE SOURCE: Upjohn Co., Kalamazoo, MI, USA
 SOURCE: Recent Adv. Chemother., Proc. Int. Congr. Chemother.,
 14th (1985), Volume Anticancer Sect. 1, 572-3.
 Editor(s): Ishigami, Joji. Univ. Tokyo Press: Tokyo,
 Japan.
 CODEN: 55GNAX
 DOCUMENT TYPE: Conference; General Review
 LANGUAGE: English
 GI



I

AB The biol. and biochem. activities of some analogs of the highly potent but toxic antitumor antibiotic ML-1065 (I) [69866-21-3] are compared to their DNA binding properties. In general, the binding affinity correlates with potency in the P388 activity and the degree of inhibition of L1210 cell growth and macromol. synthesis.

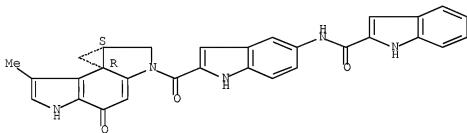
IT 101222-80-4 104713-39-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antitumor activity of and DNA binding by and DNA formation response to)

RN 101222-80-4 CAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[[(7bR, 8aS)-4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl]carbonyl]-1H-indol-5-yl]-
(CA INDEX NAME)

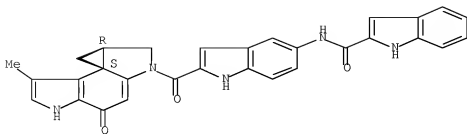
Absolute stereochemistry. Rotation (+).



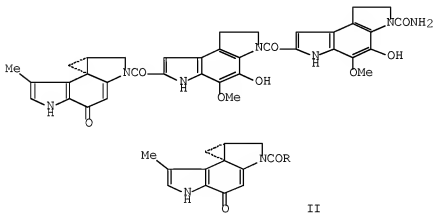
RN 104713-39-5 CAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[[(7bS, 8aR)-4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl]carbonyl]-1H-indol-5-yl]-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



17 ANSWER 181 OF 183 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1987:291 CAPLUS Full-text
DOCUMENT NUMBER: 106:291
ORIGINAL REFERENCE NO.: 106:55a
TITLE:
N-2-substituted tetrahydro-4-oxocyclopropa[c]pyrrolo[3,2-e]indoles: novel anticancer agents modeled on CC-1065
AUTHOR(S): Warpehowski, M. A.; Kelly, R. C.; McGovren, J. P.; Wierenga, W.
CORPORATE SOURCE: Upjohn Co., Kalamazoo, MI, USA
SOURCE: Recent Adv. Chemother., Proc. Int. Congr. Chemother., 14th (1985), Volume Anticancer Sect. 1, 570-1.
Editor(s): Ishigami, Joji. Univ. Tokyo Press: Tokyo, Japan.
CODEN: 55GNAX
DOCUMENT TYPE: Conference
LANGUAGE: English
GI



AB The antitumor activity of ML-1065 (I) [69866-21-3] and its analogs II (R = Me, 2-quinolinyl, 2-pyrrolyl, 2-indolyl, etc.) is described. Analogs with acyl, aroyl, and heteroaroyl substituents on N-2 of II had generated 2 highly active subgroups differentiated by DNA binding. Several DNA-binding analogs

exhibited similar potency to I but significantly improved antitumor activity (murine and human) with an absence of delayed lethality.

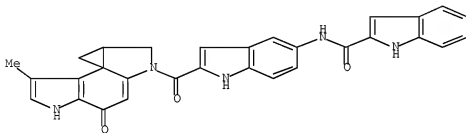
IT 104713-40-8

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antitumor activity of)

RN 104713-40-8 CAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[(4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl)carbonyl]-1H-indol-5-yl]-(CA INDEX NAME)



L7 ANSWER 182 OF 183 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1986:564557 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 105:164557

ORIGINAL REFERENCE NO.: 105:26357a,26360a

TITLE: Antitumor activity and biochemistry of novel analogs of the antibiotic, CC-1065

AUTHOR(S): Wierenga, W.; Bhuyan, B. K.; Kelly, R. C.; Krueger, W. C.; Li, L. H.; McGovren, J. P.; Swenson, D. H.; Warpehoski, M. A.

CORPORATE SOURCE: Upjohn Co., Kalamazoo, MI, 49001, USA

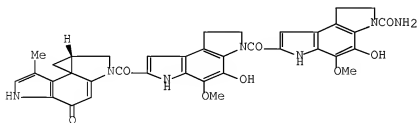
SOURCE: Advances in Enzyme Regulation (1986), 25, 141-55

CODEN: AEZRA2; ISSN: 0065-2571

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

GI



I

AB A discussion on the in vitro and in vivo antitumor activities of ML-1065 (I) [69866-21-3] and its analogs is presented. The effects of these compds. on

macromol. (DNA, protein, and RNA) biosynthesis and cell cycle are discussed.
A review of previous work is included.

IT 101222-80-4 104713-39-5 104713-40-8

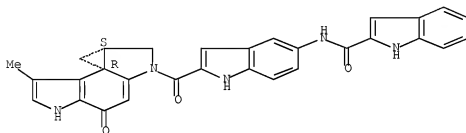
RL: PRP (Properties)

(antitumor activity and biochem. effects of, in humans and lab.
animals)

RN 101222-80-4 CAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[[(7bR,8aS)-4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl]carbonyl]-1H-indol-5-yl]-
(CA INDEX NAME)

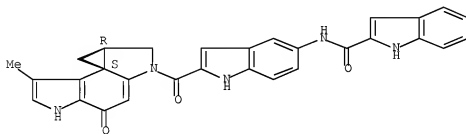
Absolute stereochemistry. Rotation (+).



RN 104713-39-5 CAPLUS

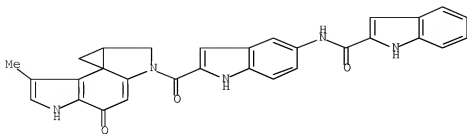
CN 1H-Indole-2-carboxamide, N-[2-[[(7bS,8aR)-4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl]carbonyl]-1H-indol-5-yl]-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 104713-40-8 CAPLUS

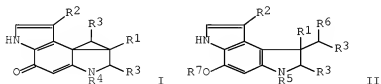
CN 1H-Indole-2-carboxamide, N-[2-[[(4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl]carbonyl]-1H-indol-5-yl]-
(CA INDEX NAME)



L7 ANSWER 183 OF 183 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 1986:148641 CAPLUS Full-text
 DOCUMENT NUMBER: 104:148641
 ORIGINAL REFERENCE NO.: 104:23517a,23520a
 TITLE: Analogs of antibiotic CC-1065
 INVENTOR(S): Kelly, Robert Charles; Warpehoski, Martha Ann;
 Wierenga, Wendell
 PATENT ASSIGNEE(S): Upjohn Co. , USA
 SOURCE: Eur. Pat. Appl., 96 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 154445	A1	19850911	EP 1985-301125	19850220
EP 154445	B1	19890531		
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
US 4912227	A	19900327	US 1986-894314	19860807
JP 08225573	A	19960903	JP 1995-331640	19951220
PRIORITY APPLN. INFO.:			US 1984-581836	A 19840221
			US 1985-694363	A 19850124
			CA 1985-473917	A 19850208
			ZA 1985-1093	A 19850213
			EP 1985-301125	A 19850220
			JP 1985-31662	A 19850221

GI



AB Title compds. I and II (R1, R2, R3 = H, alkyl, phenyl; R4 = H, acyl; R5 = acyl; R6 = halo, substituted sulfonyloxy; R7 = Me, substituted Me) and their salts, useful as UV light absorbers, bactericides, and antitumors were prepd.

Thus, II (R1 = R2 = R3 = H, R5 = mesyl, R7 = PhCH2) was N-demethylated, N-acetylated, O-mesylated, O-debenzylated, and cyclized to give I (R1 = R2 = R3 = H, R4 = Ac). The latter compd. showed cytotoxic activity against murine L1210 tumor cells at 0.0048 .mu.g/mL.

IT 101134-75-2P 101134-79-6P 101134-83-2P

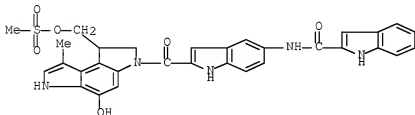
101134-84-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and cyclization of)

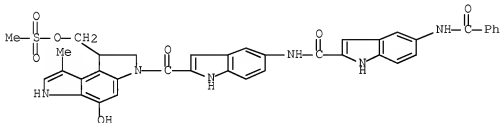
RN 101134-75-2 CAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[[1,6-dihydro-5-hydroxy-8-methyl-1-[[(methylsulfonyl)oxy]methyl]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



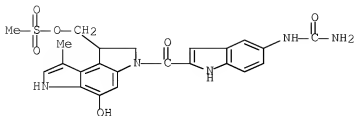
RN 101134-79-6 CAPLUS

CN 1H-Indole-2-carboxamide, 5-(benzoylamino)-N-[2-[[1,6-dihydro-5-hydroxy-8-methyl-1-[[(methylsulfonyl)oxy]methyl]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



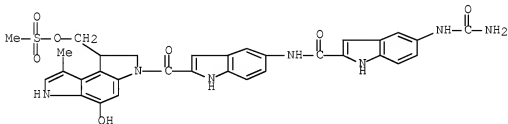
RN 101134-83-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol, 3-[[5-[(aminocarbonyl)amino]-1H-indol-2-yl]carbonyl]-1,2,3,6-tetrahydro-5-hydroxy-8-methyl-, .alpha.-methanesulfonate (9CI) (CA INDEX NAME)



RN 101134-84-3 CAPLUS

CN 1H-Indole-2-carboxamide, 5-[(aminocarbonyl)amino]-N-[2-[[1,6-dihydro-5-hydroxy-8-methyl-1-[[[(methylsulfonyl)oxy]methyl]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]]- (9CI) (CA INDEX NAME)



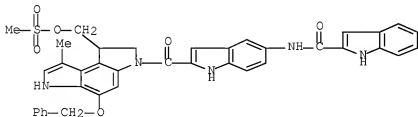
IT 101134-61-6P 101134-62-7P 101134-63-8P

101134-65-8P

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(prepn. and debenzoylation of)

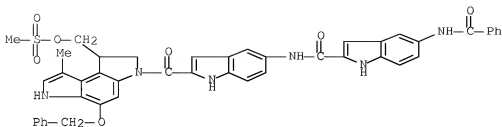
RN 101134-61-6 CAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[[1,6-dihydro-8-methyl-1-[[[(methylsulfonyl)oxy]methyl]-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]]- (9CI) (CA INDEX NAME)



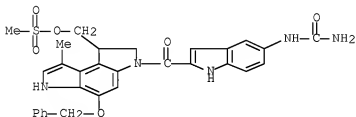
RN 101134-62-7 CAPLUS

CN 1H-Indole-2-carboxamide, 5-(benzoylamino)-N-[2-[[1,6-dihydro-8-methyl-1-[[[(methylsulfonyl)oxy]methyl]-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]]- (9CI) (CA INDEX NAME)



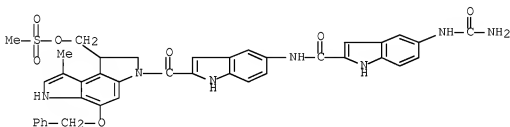
RN 101134-63-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol, 3-[[5-[(aminocarbonyl)amino]-1H-indol-2-yl]carbonyl]-1,2,3,6-tetrahydro-8-methyl-5-(phenylmethoxy)-, methanesulfonate (ester) (9CI) (CA INDEX NAME)



RN 101134-65-0 CAPLUS

CN 1H-Indole-2-carboxamide, 5-[(aminocarbonyl)amino]-N-[2-[[1,6-dihydro-8-methyl-1-[(methylsulfonyl)oxy]methyl]-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



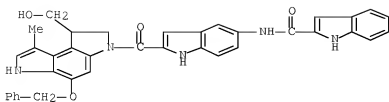
IT 101134-50-3P 101134-52-5P 101134-53-6P

101151-43-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. and mesylation of)

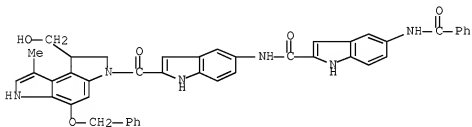
RN 101134-50-3 CAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[[1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



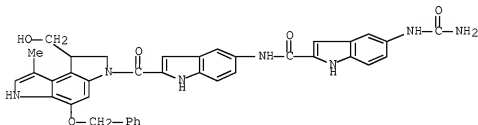
RN 101134-52-5 CAPLUS

CN 1H-Indole-2-carboxamide, 5-(benzoylamino)-N-[2-[[1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



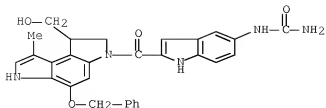
RN 101134-53-6 CAPLUS

CN 1H-Indole-2-carboxamide, 5-[(aminocarbonyl)amino]-N-[2-[[1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



RN 101151-43-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol, 3-[[5-[(aminocarbonyl)amino]-1H-indol-2-yl]carbonyl]-1,2,3,6-tetrahydro-8-methyl-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



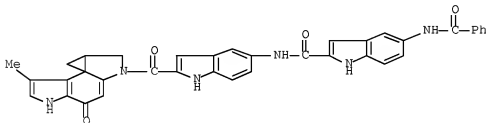
IT 101134-80-9P 101151-46-6P 101151-47-7P

101222-80-4P 104713-40-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antitumor and antibiotic)

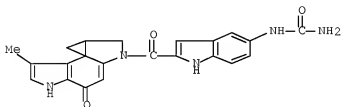
RN 101134-80-9 CAPLUS

CN 1H-Indole-2-carboxamide, 5-(benzoylamino)-N-[2-[(4,5,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl)carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)



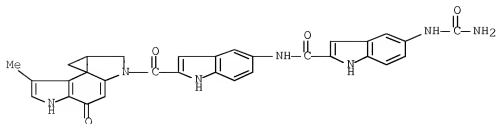
RN 101151-46-6 CAPLUS

CN Cyclopropa[c]pyrrolo[3,2-e]indol-4(5H)-one, 2-[[5-[(aminocarbonyl)amino]-1H-indol-2-yl]carbonyl]-1,2,8,8a-tetrahydro-7-methyl- (9CI) (CA INDEX NAME)



RN 101151-47-7 CAPLUS

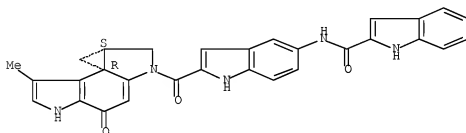
CN 1H-Indole-2-carboxamide, 5-[(aminocarbonyl)amino]-N-[2-[(4,5,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl)carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)



RN 101222-80-4 CAPLUS

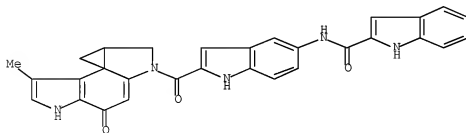
CN 1H-Indole-2-carboxamide, N-[2-[(7bR,8aS)-4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl]carbonyl]-1H-indol-5-yl)-(CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 104713-40-8 CAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[(4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl]carbonyl]-1H-indol-5-yl)-(CA INDEX NAME)



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	ENTRY	SESSION
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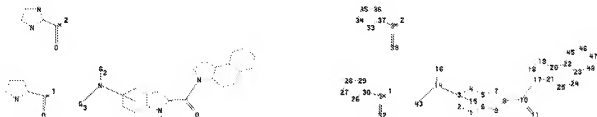
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chain nodes :
10 11 13 14 16 31 32 38 39 43
ring nodes :
1 2 3 4 5 6 7 8 9 17 18 19 20 21 22 23 24 25 26 27 28 29 30
33 34 35 36 37 45 46 47 48
chain bonds :
8-10 9-13 10-11 10-17 14-16 14-43 30-31 31-32 37-38 38-39
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 17-18 17-21 18-19 19-20 20-21
20-22 21-25 22-23 22-45 23-24 23-48 24-25 26-27 26-30 27-28 28-29 29-30
33-34 33-37
34-35 35-36 36-37 45-46 46-47 47-48
exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 9-13 10-11 10-17 14-16 14-43
17-18 17-21 18-19 19-20 20-21 20-22 21-25 22-23 22-45 23-24 23-48 24-25

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26-27 26-30
 27-28 28-29 29-30 31-32 33-34 33-37 34-35 35-36 36-37 38-39 45-46 46-47
 47-48
 exact bonds :
 8-10 30-31 37-38
 isolated ring systems :
 containing 26 : 33 :

G2:H,CH,t-Bu

G3:[*1],[*2]

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
 11:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:Atom 18:Atom 19:Atom
 20:Atom 21:Atom 22:Atom
 23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 31:CLASS
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L8 STRUCTURE UPLOADED

=> d

L8 HAS NO ANSWERS

L8 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED - 228 TO ITERATE

100.0% PROCESSED 228 ITERATIONS

1 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 3655 TO 5465

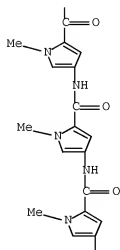
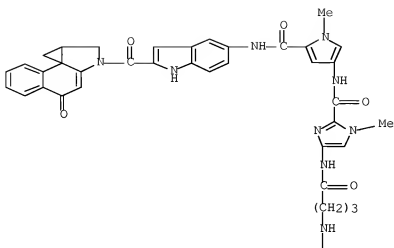
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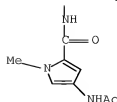
L9 1 SEA SSS SAM L8

=> d scan

L9 1 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN

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ALL ANSWERS HAVE BEEN SCANNED

=> s l8 full

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FULL SCREEN SEARCH COMPLETED - 4127 TO ITERATE

100.0% PROCESSED 4127 ITERATIONS

39 ANSWERS

SEARCH TIME: 00.00.01

L10

39 SEA SSS FUL L8

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COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

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SINCE FILE

TOTAL

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SESSION

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FILE LAST UPDATED: 7 Jul 2008 (20080707/ED)

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L11 16 L10

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L11 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2008:492970 CAPLUS Full-text

TITLE: Sequence-specific alkylation by Y-shaped and tandem hairpin pyrrole-imidazole polyamides

AUTHOR(S): Sasaki, Shunta; Bando, Toshikazu; Minoshima, Masafumi; Shinohara, Ken-ichi; Sugiyama, Hiroshi

CORPORATE SOURCE: Department of Chemistry, Kyoto University, Kitashirakawa-Oiwakekyo, Sakyo, Kyoto, 606-8502, Japan
Chemistry--A European Journal (2008), 14(3), 864-870
CODEN: CEUJED; ISSN: 0947-6539

PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To extend the target DNA sequence length of the hairpin pyrrole-imidazole (Py-Im) polyamide 1, the authors designed and synthesized Y-shaped and tandem hairpin Py-Im polyamides 2 and 3, which possess 1-(chloromethyl)-5-hydroxy-1,2-dihydro-3H-benz[e]indole (seco-CBI) as DNA-alkylating moieties. High-resolution denaturing polyacrylamide gel electrophoresis by using 5'-Texas-Red-labeled 465 base pair (bp) DNA fragments revealed that conjugates 2 and 3 alkylated the adenine of the target DNA sequences at nanomolar concns. Conjugate 2 alkylated adenine N3 at the 3' end of two 8 bp match sequences, 5'-AA- TAACCA-3' (site A) and 5'-AAATTC-CA-3' (site C), while conjugate 3 recognized one 10 bp match sequence, 5'-AGAATAACCA-3' (site A) in the 465 bp DNA fragments. These results demonstrate that seco-CBI conjugates of Y-shaped and tandem hairpin polyamides have extended their target alkylation sequences.

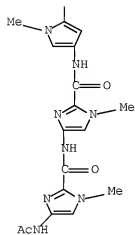
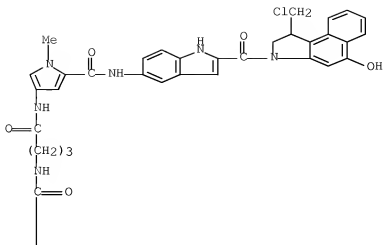
IT INDEXING IN PROGRESS

IT 1032252-71-3P 1032252-73-5P 1032252-75-7P

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(solid-phase prepn. of tandem hairpin pyrrole-imidazole polyamides, evaluation of their DNA-alkylating capabilities and cytotoxicity in human cancer cell lines)

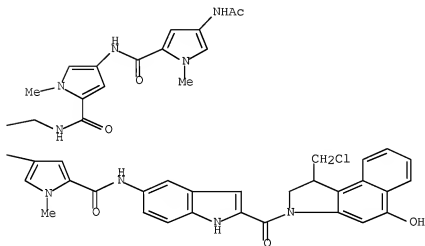
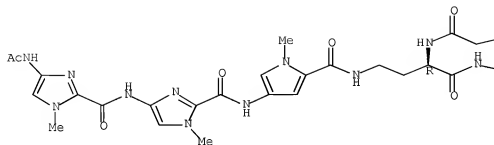
RN 1032252-71-3 CAPLUS

CN INDEX NAME NOT YET ASSIGNED



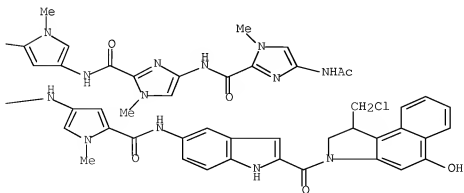
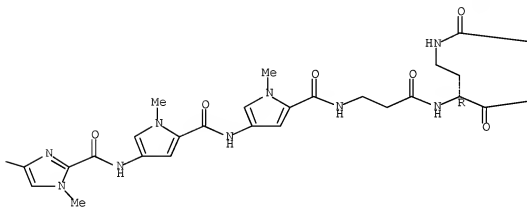
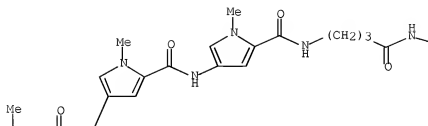
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CN INDEX NAME NOT YET ASSIGNED

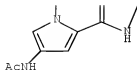
Absolute stereochemistry.



RN 1032252-75-7 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.





REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2008 ACS ON STN

ACCESSION NUMBER: 2008:339576 CAPLUS Full-text

DOCUMENT NUMBER: 148:555820

TITLE: Requirement of .beta.-alanine components in sequence-specific DNA alkylation by pyrrole-imidazole conjugates with seven-base pair recognition

AUTHOR(S): Bando, Toshikazu; Minoshima, Masafumi; Kashiwazaki, Gengo; Shinohara, Ken-ichi; Sasaki, Shunta; Fujimoto, Jun; Ohtsuki, Akimichi; Murakami, Masataka; Nakazono, Satomi; Sugiyama, Hiroshi

CORPORATE SOURCE: Department of Chemistry, Graduate School of Science, Kyoto University, Sakyo, Kyoto, 606-8501, Japan

SOURCE: Bioorganic & Medicinal Chemistry (2008), 16(5), 2286-2291

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To investigate the effect of incorporation of .beta.-alanine in alkylating N-methylpyrrole (Py)-N-methylimidazole (Im) polyamide, seco-CBI conjugates 2-8 were synthesized by an Fmoc solid-phase method and subsequent coupling with an alkylating moiety. DNA-alkylating activities of conjugates 2-8 were evaluated by high-resoln. denaturing gel electrophoresis with 202-base pair (bp) DNA fragments. Alkylation by conjugates 2 and 3, which have antiparallel pairings of .beta.-alanine (.beta.) opposite .beta. (.beta./beta.) and Py/beta., occurred mainly at the adenine (A) of the matching sequences, 5'-AGCTCC-3' (site 1) and 5'-AGCACC-3' (site 3). However, conjugate 4, with .beta./Py, did not show any DNA-alkylating activities. Similarly, conjugate 5, which possessed a Py/Py pair, weakly alkylated the matching sites at micromolar concns. Conjugates 6 and 7, which possessed .beta./beta. and Py/beta. pairs, resp., alkylated at the A of the matching sequences, 5'-ACTACC-3' (site 2) and 5'-ACAACC-3' (site 4). In contrast, conjugated 8, with a Py/Py pair, showed lower activity and less alkylated DNA at sites 2 and 4 with mismatched alkylation at site 1 at a higher concn. than that of 6 and 7. These results demonstrate that incorporation of .beta.-alanine is required for the sequence-specific alkylation by seco-CBI Py-Im conjugates with a seven-base pair sequence.

IT 865113-72-0P 1026780-43-2P 1026780-50-6P

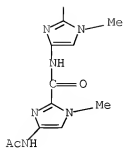
1026780-52-8P 1026780-53-3P 1026780-54-0P

RL: BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP

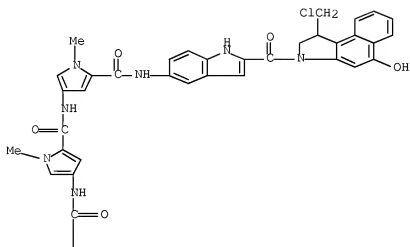
RN 865113-72-0 CAPLUS

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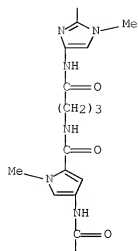
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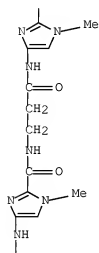
RN 1026780-48-2 CAPLUS
CN INDEX NAME NOT YET ASSIGNED



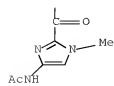
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PAGE 3-A

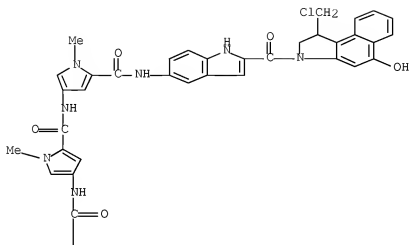


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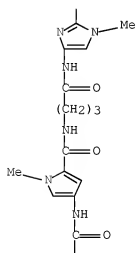


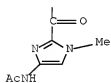
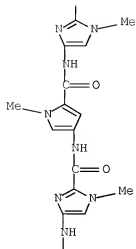
RN 1026780-50-6 CAPLUS
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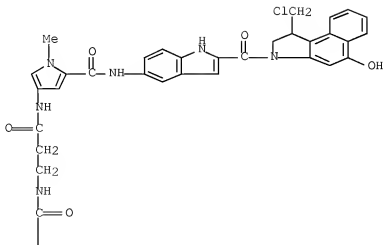


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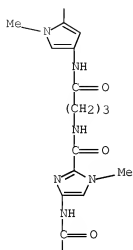




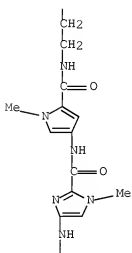
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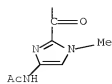


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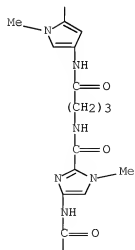
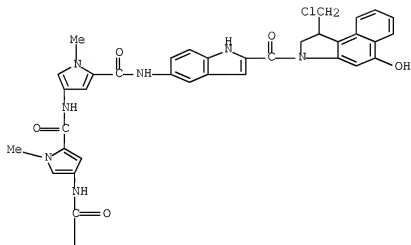


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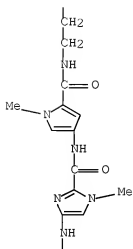




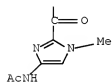
RN 1026780-53-9 CAPLUS
 CN INDEX NAME NOT YET ASSIGNED



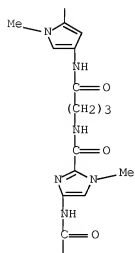
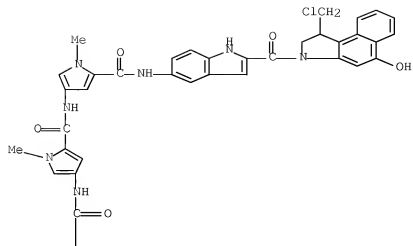
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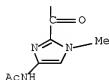
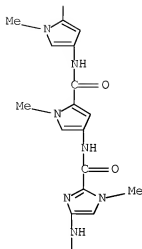


PAGE 4-A



RN 1026780-54-0 CAPLUS
CN INDEX NAME NOT YET ASSIGNED





REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2007:662474 CAPLUS [Full-text](#)
 DOCUMENT NUMBER: 147:323219
 TITLE: Molecular design of DNA alkylating pyrrole-imidazole polyamides with longer recognition sequence
 AUTHOR(S): Minoshima, Masafumi; Sasaki, Shunta; Shinohara, Ken-ichi; Shimizu, Tatsuhiko; Bando, Toshikazu; Sugiyama, Hiroshi
 CORPORATE SOURCE: Department of Chemistry, Graduate School of Science, Kyoto University, Kitashirakawa-oiwakecho, Sakyo, Kyoto, 606-8502, Japan
 SOURCE: Nucleic Acids Symposium Series (2006), (50), 165-166
 CODEN: NASSCJ
 URL: <http://nass.oxfordjournals.org/content/vol50/issue1/index.dtl>
 PUBLISHER: Oxford University Press
 DOCUMENT TYPE: Journal; (online computer file)
 LANGUAGE: English
 AB The sequence-specificity, and DNA alkylating activity of the conjugate 1, which consists of N-methylpyrrole (Py)-N-methylimidazole (Im) polyamides, 1-(chloromethyl)-5-hydroxy-1,2-dihydro-3H-benz[e]indole (seco-CBI) with indole

linker, were investigated in the absence or presence of partner Py-Im polyamide 2. High-resoln. denaturing PAGE showed that the specificity of DNA alkylation by 1 modulated in the presence of partner 2. We found that sequence-specific DNA alkylation by 1 and 2 with 10 base pair (bp) match recognition sequence through heterodimer formation. This result indicates one possibility of DNA alkylation with longer recognition sequence by different two mols.

IT 947726-88-7

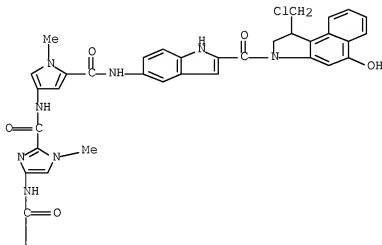
RL: BUU (Biological use, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)

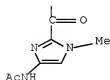
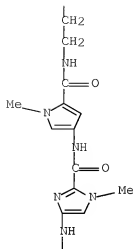
(DNA alkylating agent; sequence-specific alkylation of DNA with pyrrole-imidazole polyamide seco-CBI conjugate in presence of partner polyamide)

RN 947726-88-7 CAPLUS

CN 1H-Imidazole-2-carboxamide, 4-[[[4-(acetylamino)-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-N-[5-[[[3-[[2-[[[5-[[[2-[[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]-3-oxopropyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl- (CA INDEX NAME)

PAGE 1-A





REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2007:662469 CAPLUS [Full-text](#)
 DOCUMENT NUMBER: 148:182769
 TITLE: Synthesis and evaluation of sequence-specific DNA alkylating agents: effect of alkylation subunits
 AUTHOR(S): Shimizu, Tatsuhiko; Sasaki, Shunta; Minoshima, Masafumi; Shinohara, Ken-ichi; Bando, Toshikazu; Sugiyama, Hiroshi
 CORPORATE SOURCE: Department of Chemistry, Graduate School of Science, Kyoto University, Kitashirakawa Oiwakecho, Sakyo-ku, Kyoto, 606-8502, Japan
 SOURCE: Nucleic Acids Symposium Series (2006), (50), 155-156
 CODEN: NASSCJ
 URL: <http://nass.oxfordjournals.org/content/vol50/issue1/index.dtl>
 PUBLISHER: Oxford University Press
 DOCUMENT TYPE: Journal; (online computer file)
 LANGUAGE: English
 AB We have demonstrated that hairpin pyrrole (Py)-imidazole (Im) polyamide-CBI conjugates selectively alkylate predetd. sequences. In this study, we investigated the effect of alkylation subunits, for example conjugates 1-4

with three types of DNA alkylating units, and Py-Im polyamides with indole linker. Conjugate 3 and 4 selectively alkylated the predetd. sequences as described previously, while conjugates 1 and 2 alkylate at mismatched sites.

IT 865113-72-8 1084312-35-9

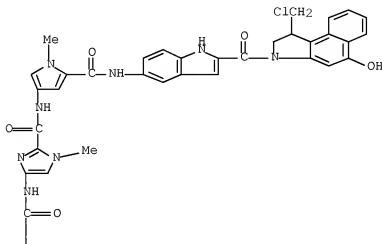
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

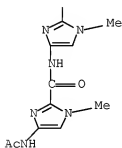
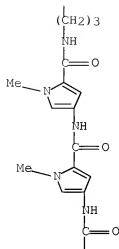
(sequence-specific DNA alkylating agents as antitumor drugs with improved selectivity)

RN 865113-72-0 CAPLUS

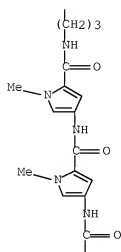
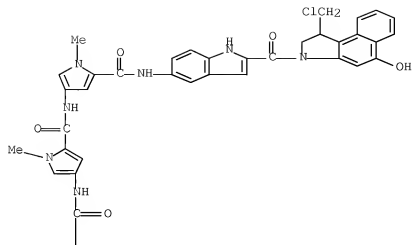
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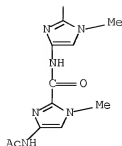
PAGE 1-A





RN 1004312-35-9 CAPLUS
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 1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]-1-methyl- (CA
 INDEX NAME)





REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:662447 CAPLUS Full-text

DOCUMENT NUMBER: 147:316628

TITLE: The biological impact of sequence-specific DNA alkylation by pyrroleimidazole polyamides

AUTHOR(S): Sasaki, Shunta; Minoshima, Masafumi; Shimizu, Tatsuhiko; Fujimoto, Jun; Shinohara, Ken-ichi; Bando, Toshikazu; Sugiyama, Hiroshi

CORPORATE SOURCE: Department of Chemistry, Graduate School of Science, Kyoto University, Kitashirakawa Oiwake, Sakyo-ku, Kyoto, 606-8502, Japan

SOURCE: Nucleic Acids Symposium Series (2006), (50), 111-112
CODEN: NASSCJ

URL: <http://nass.oxfordjournals.org/content/vol50/issue1/index.dtl>

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

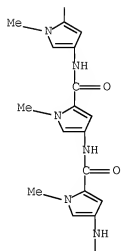
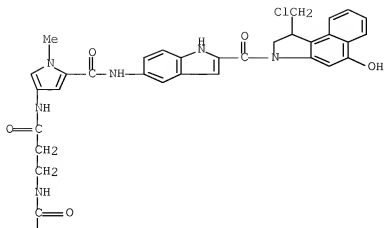
AB We have developed a series of novel DNA alkylating polyamides possessing indole linkers. Investigations using high-resoln. gel electrophoresis revealed that the indole linked Py-Im polyamide alkylated at A of a targeted nine base pair matching sequence. Evaluation in human cancer cell lines revealed that the indole linked Py-Im polyamides have strong cytotoxicities. Furthermore, we showed that alkylation of the template strand of the coding region by these polyamides causes effective gene silencing.

IT 993419-09-5P 947597-79-7P 947597-85-5P
947597-99-1P

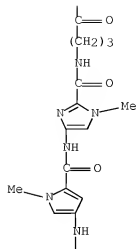
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation);
BIOL (Biological study); PREP (Preparation)
(biol. impact of sequence-specific DNA alkylation by pyrroleimidazole polyamides)

RN 993419-09-5 CAPLUS

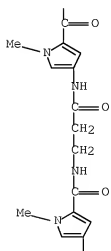
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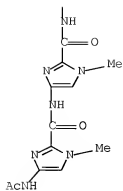


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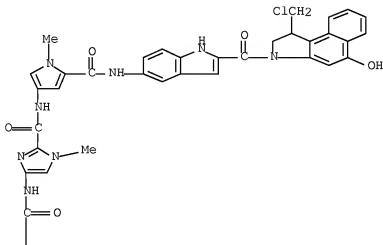
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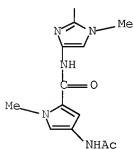
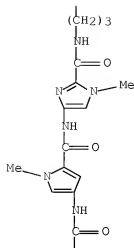




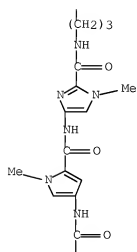
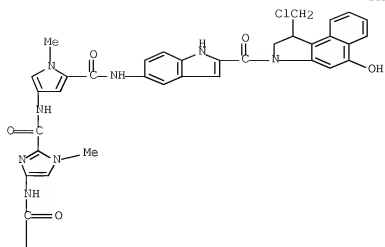
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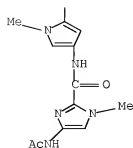
CN 1H-Imidazole-2-carboxamide, 4-[[[4-[[[4-[(acetylamino)-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-N-[4-[[2-[[[5-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]-4-oxobutyl]-1-methyl- (CA INDEX NAME)



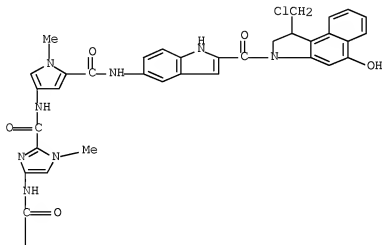


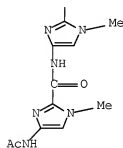
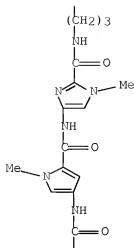
RN 947597-85-5 CAPLUS
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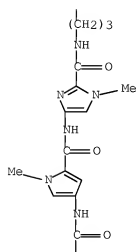
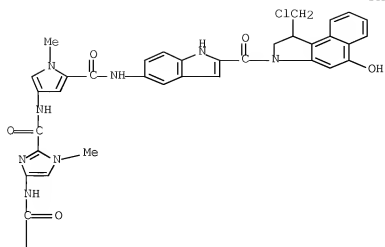


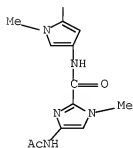
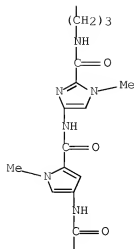
RN 947597-99-1 CAPLUS
 CN 1H-Imidazole-2-carboxamide, 4-[[[4-(acetylamino)-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-N-[5-[[[2-[[[4-[[2-[[[5-[[[2-[[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]-4-oxobutyl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl- (CA INDEX NAME)





IT 947597-72-6P 947597-93-5P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (biol. impact of sequence-specific DNA alkylation by pyrroleimidazole
 polyamides)
 RN 947597-72-0 CAPLUS
 CN 1H-Imidazole-2-carboxamide, 4-[[[4-[[[4-[[[4-(acetamino)-1-methyl-1H-
 pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-
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 (chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-
 indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-
 methyl-1H-imidazol-4-yl]amino]-4-oxobutyl]-1-methyl- (CA INDEX NAME)





REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2007:662248 CAPLUS Full-text
 DOCUMENT NUMBER: 147:315627
 TITLE: Sequence-specific gene silencing by alkylating Py-Im polyamide
 AUTHOR(S): Shinohara, Ken-ichi; Sasaki, Shunta; Bando, Toshikazu; Sugiyama, Hiroshi
 CORPORATE SOURCE: Graduate School of Science, Kyoto University, Kitashirakawa Oiwakecho, Sakyo-ku, Kyoto, 606-8502, Japan
 SOURCE: Nucleic Acids Symposium Series (2005), (49), 75-76
 CODEN: NASSCJ
 URL: <http://nass.oxfordjournals.org/content/vol49/issue1/index.dtl>
 PUBLISHER: Oxford University Press
 DOCUMENT TYPE: Journal; (online computer file)
 LANGUAGE: English

AB We have demonstrated that hairpin pyrrole (Py)-imidazole (Im) polyamide-CPI conjugates selectively induced luciferase gene silencing by sequence-specific alkylation of the coding region. Recently, we developed a new type of Py-Im polyamide CBI conjugate with an indole linker as a stable sequence-specific alkylating agent. In this study, we investigated the gene silencing ability of polyamides A, B and C, which potentially target specific sequences in the promoter region, noncoding strand, and coding strand of the green fluorescent protein (GFP) gene, resp. The GFP vectors were transfected into human colon carcinoma cells (HCT116), and the cells treated with 100 nM of the polyamides for 24 h. Using direct observation of cell by fluorescence microscopy, a significant GFP-gene silencing effect was only seen with treatment with polyamide C. Polyamides A and B did not show such activity.

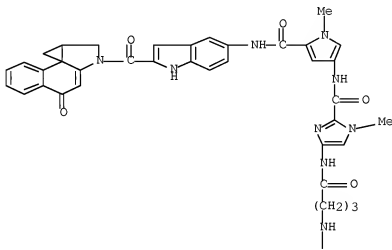
IT 865113-64-0 865113-67-3 885028-77-3

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sequence-specific green fluorescent protein gene silencing in human cells by alkylating Py-Im polyamide)

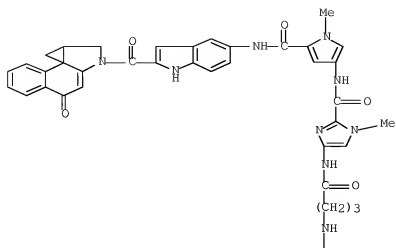
RN 865113-64-0 CAPLUS

CN 1H-Imidazole-2-carboxamide, 4-[[[4-(acetylamino)-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-N-[5-[[[5-[[[4-[[2-[[[5-[[[2-[[[9,9a-dihydro-4-oxo-1H-benzo[e]cycloprop[c]indol-2(4H)-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]-4-oxobutyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl- (CA INDEX NAME)

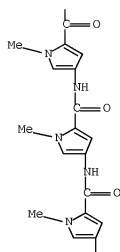
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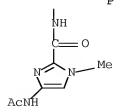
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PAGE 2-A



PAGE 3-A

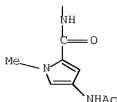


CN

CN

Chemical structure of compound 10: A complex molecule featuring a fluorenyl group linked via an amide bond to a benzimidazole ring, which is further linked to a 2-methyl-5-((2-methyl-1H-imidazol-2-yl)carbamoyl)-1H-imidazole-4-carboxamide moiety.

Cc1cc(C(=O)Nc2cc(C)nn2)nn1C(=O)Nc3cc(C)nn3C(=O)Nc4cc(C)nn4



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2008 ACS ON STN
 ACCESSION NUMBER: 2007:662158 CAPLUS Full-text
 DOCUMENT NUMBER: 148:517913
 TITLE: Molecular design of alkylating pyrrole-imidazole polyamides with indole linker
 AUTHOR(S): Sasaki, Shunta; Narita, Akihiko; Bando, Toshikazu; Sugiyama, Hiroshi
 CORPORATE SOURCE: School of Biomedical Science, Tokyo Medical and Dental University, 2-3-10 Kanda-Surugadai, Chiyodaku, Tokyo, 101-0062, Japan
 SOURCE: Nucleic Acids Symposium Series (2004), (48), 205-206
 CODEN: NASSCJ
 URL: <http://nass.oxfordjournals.org/content/vol48/issue1/index.dtl>
 PUBLISHER: Oxford University Press
 DOCUMENT TYPE: Journal; (online computer file)
 LANGUAGE: English

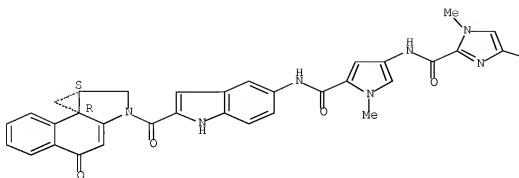
AB A series of novel DNA alkylating polyamide possessing indole linker was synthesized. The reactivities and specificities of these polyamides with double strand DNA were investigated by using high-resoln. gel electrophoresis. The results revealed that the indole linker linked Py-Im polyamides have the high alkylating activities and sequence specificities comparable to vinyl linker linked Py-Im polyamides.

IT 1021452-23-2P 1021452-26-5P 1021452-29-8P
 1021452-32-3P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (mol. design of alkylating pyrrole-imidazole polyamides with indole linker)

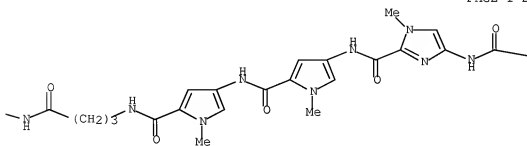
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 CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.

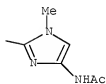
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PAGE 1-B



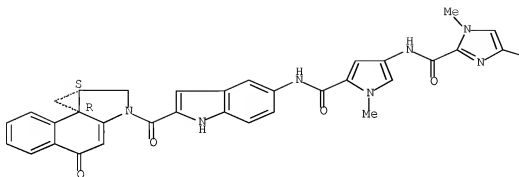
PAGE 1-C



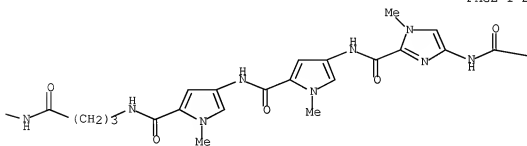
RN 1021452-26-5 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.

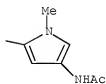
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PAGE 1-B

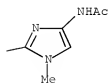
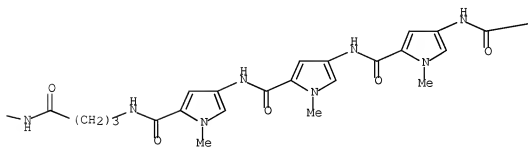
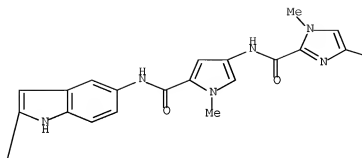


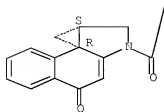
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RN 1021452-29-8 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

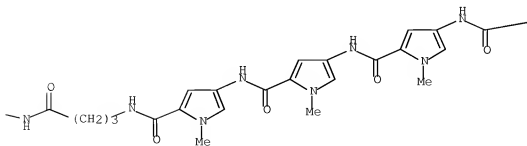
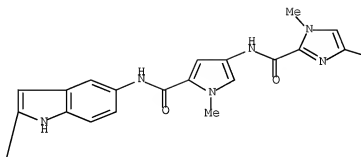
Absolute stereochemistry.

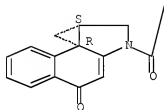
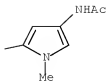




RN 1021452-32-3 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.





REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:408268 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 147:47403

TITLE: DNA Alkylation by Pyrrole-Imidazole seco-CBI Conjugates with an Indole Linker: Sequence-Specific DNA Alkylation with 10-Base-Pair Recognition through Heterodimer Formation

AUTHOR(S): Minoshima, Masafumi; Bando, Toshikazu; Sasaki, Shunta; Shinohara, Ken-ichi; Shimizu, Tatsuhiko; Fujimoto, Jun; Sugiyama, Hiroshi

CORPORATE SOURCE: Department of Chemistry, Graduate School of Science, Kyoto University, Sakyo, Kyoto, 606-8502, Japan

SOURCE: Journal of the American Chemical Society (2007), 129(17), 5384-5390

CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 147:47403

AB The sequence-specific DNA alkylation by conjugates 4 and 5, which consist of N-methylpyrrole (Py)-N-methylimidazole (Im) polyamides and 1-(chloromethyl)-5-hydroxy-1,2-dihydro-3H-benz[e]indole (seco-CBI) linked with an indole linker, was investigated in the absence or presence of partner Py-Im polyamide 6. High-resoln. denaturing PAGE revealed that conjugate 4 alkylates DNA at the sequences 5'-(A/T)GCCTA-3' through hairpin formation, and alkylates 5'-GGAAAGAAAA-3' through an extended binding mode. However, in the presence of partner Py-Im polyamide 6, conjugate 4 alkylates DNA at a completely different sequence, 5'-AGGTTGTCCA-3'. Alkylation of 4 in the presence of 6 was effectively inhibited by a competitor 7. Surface plasmon resonance (SPR) results indicated that conjugate 4 does not bind to 5'-AGGTTGTCCA-3', whereas 6 binds tightly to this sequence. The results suggest that alkylation proceeds through heterodimer formation, indicating that this is a general way

to expand the recognition sequence for DNA alkylation by Py-Im seco-CBI conjugates.

IT 939435-69-5P 939435-70-8P

RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

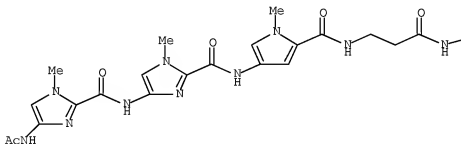
(sequence-specific DNA alkylation by pyrrole-imidazole seco-CBI conjugates with an indole linker)

RN 939435-69-5 CAPLUS

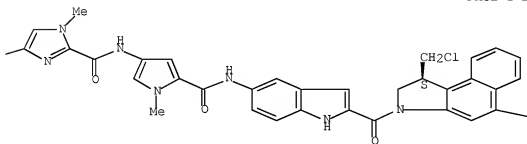
CN 1H-Imidazole-2-carboxamide, 4-[[[4-(acetylamino)-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-N-[5-[[[3-[[2-[[[5-[[2-[[[1S]-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]-3-oxopropyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



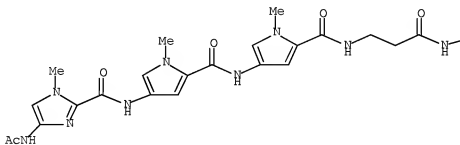
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RN 939435-70-8 CAPLUS

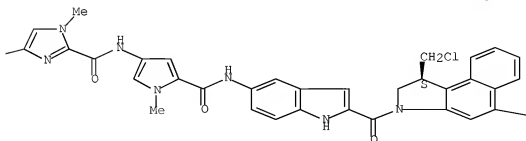
CN 1H-Imidazole-2-carboxamide, 4-(acetylamino)-N-[5-[[[5-[[[3-[[2-[[[5-[[[2-
[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-
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yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]-3-
oxopropyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-
1H-pyrrol-3-yl]-1-methyl- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



OH

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2008 ACS ON STN
 ACCESSION NUMBER: 2006:860352 CAPLUS Full-text
 DOCUMENT NUMBER: 145:448749
 TITLE: Sequence-Specific Alkylation of Double-Strand Human
 Telomere Repeat Sequence by Pyrrole-Imidazole
 Polyamides with Indole Linkers
 AUTHOR(S): Sasaki, Shunta; Bando, Toshikazu; Minoshima, Masafumi;
 Shimizu, Tatsuhiko; Shinohara, Ken-Ichi; Takao, Toshiyasu; Sugiyama, Hiroshi
 CORPORATE SOURCE: Department of Chemistry, Graduate School of Science,
 Kyoto University, Kyoto, 606-8502, Japan
 SOURCE: Journal of the American Chemical Society (2006),
 128(37), 12162-12168
 CODEN: JACSAT; ISSN: 0002-7863
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 145:448749
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

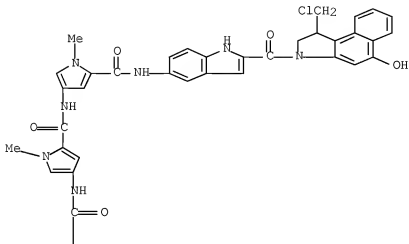
AB The authors designed and synthesized pyrrole (Py)-imidazole (Im) hairpin polyamide 1-(chloromethyl)-5-hydroxy-1,2-dihydro-3H-benz[e]indole (seco-CBI) conjugates which target both strands of the double-stranded region of the human telomere repeat sequences, 5'-d(TTAGGG)n-3'/5'-d(CCTAA)n-3'. High-resoln. denaturing PAGE demonstrated that the conjugates alkylated DNA at the 3' A of 5'-ACCCTA-3' and 5'-AGGGTTA-3', resp. Cytotoxicities of the conjugates were evaluated using 39 human cancer cell lines; avs. of log IC50 values for these conjugates were -6.96 (110 nM) and -7.24 (57.5 nM), resp. These conjugates have potential as antitumor drugs capable of targeting telomere repeat sequence.

IT 865113-70-3P 912552-39-7P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (sequence-specific alkylation of double-strand human telomere repeat sequence by pyrrole-imidazole polyamides with indole linkers)

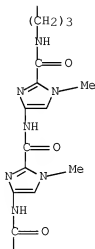
RN 865113-70-8 CAPLUS
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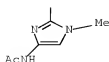
yl]carbonyl]amino]-N-[2-[[[4-[[5-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]-4-oxobutyl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]-1-methyl- (CA INDEX NAME)

PAGE 1-A

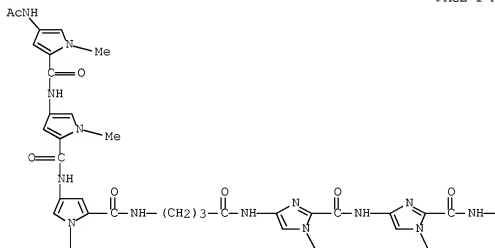


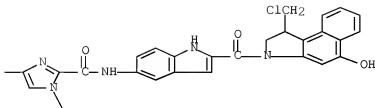
PAGE 2-A





RN 912552-39-7 CAPLUS
 CN 1H-imidazole-2-carboxamide, 4-[[[4-[[[4-[[[4-[[[4-(acetamido)-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-N-[2-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]-1-methyl- (CA INDEX NAME)





REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

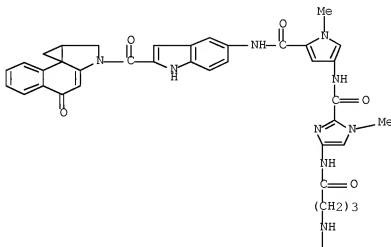
L11 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2006:385992 CAPLUS Full-text
 DOCUMENT NUMBER: 145:103905
 TITLE: Efficient DNA Alkylation by a Pyrrole-Imidazole CBI Conjugate with an Indole Linker: Sequence-Specific Alkylation with Nine-Base-Pair Recognition
 AUTHOR(S): Bando, Toshikazu; Sasaki, Shunta; Minoshima, Masafumi; Dohno, Chikara; Shinohara, Ken-Ichi; Narita, Akihiko; Sugiyama, Hiroshi
 CORPORATE SOURCE: Department of Chemistry, Graduate School of Science, Kyoto University, Kyoto, 606-8501, Japan
 SOURCE: Bioconjugate Chemistry (2006), 17(3), 715-720
 CODEN: BCCHEJ; ISSN: 1043-1802
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English

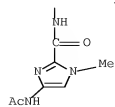
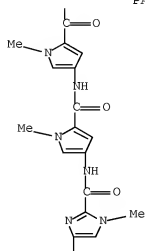
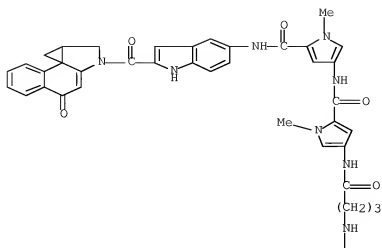
AB Conjugates of N-methylpyrrole (Py)-N-methylimidazole (Im) polyamides and 1,2,9,9a-tetrahydrocyclopropa[1,2-c]benz[1,2-e]indol-4-one (CBI) with a 5-amino-1H-indole-2-carbonyl linker were synthesized by Fmoc solid-phase synthesis and a subsequent liq.-phase coupling procedure. The DNA alkylating abilities of imidazole conjugates were examd. using Texas Red-labeled PCR fragments and high-resoln. denaturing gel electrophoresis. CBI conjugates exhibited highly efficient sequence-specific DNA alkylation comparable with previous CBI conjugates with a vinyl linker. Introduction of an indole linker greatly facilitated the synthesis of sequence-specific alkylating Py-Im polyamides.

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

RN 865113-64-0 CAPLUS

PAGE 1-A



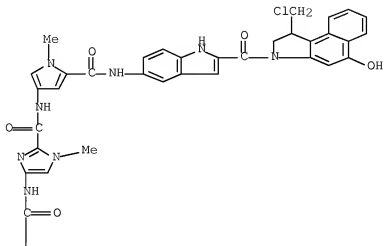


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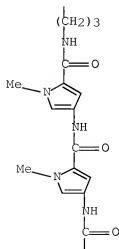
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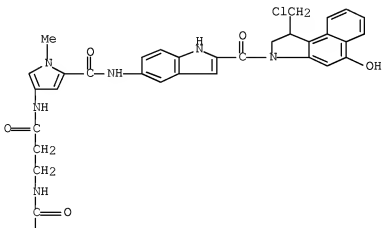
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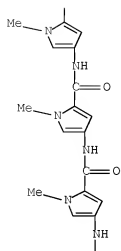
PAGE 2-A



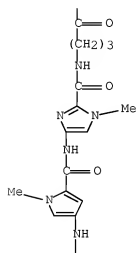
PAGE 1-A

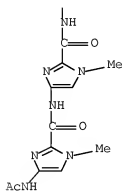
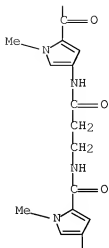


PAGE 2-A



PAGE 3-A





REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:367591 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 145:431752

TITLE: Antitumor activity of sequence-specific alkylating agents: pyrrole-imidazole CBI conjugates with indole linker

AUTHOR(S): Shinohara, Ken-ichi; Bando, Toshikazu; Sasaki, Shunta; Sakakibara, Yogo; Minoshima, Masafumi; Sugiyama, Hiroshi

CORPORATE SOURCE: Department of Chemistry, Graduate School of Science, Kyoto University, Kitashirokawa-Oiwakecho, Sakyo, Kyoto, 606-8502, Japan

SOURCE: Cancer Science (2006), 97(3), 219-225
CODEN: CSACCM; ISSN: 1347-9032

PUBLISHER: Blackwell Publishing Asia Pty Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB DNA-targeting agents, including cisplatin, bleomycin and mitomycin C, are used routinely in cancer treatments. However, these drugs are extremely toxic, attacking normal cells and causing severe side effects. One important question to consider in designing anticancer agents is whether the introduction of sequence selectivity to DNA-targeting agents can improve their efficacy as anticancer agents. In the present study, the growth inhibition activities of an indole-seco 1,2,9,9a-tetrahydrocyclopropa[1,2-c]benz[1,2-e]indol-4-one (CBI) (1) and five conjugates with hairpin pyrrole-imidazole polyamides (2-6), which have different sequence specificities for DNA alkylation, were compared using 10 different cell lines. The av. values of -log GI50 (50% growth inhibition concn.) for compds. 1-6 against the 10 cell lines were 8.33, 8.56, 8.29, 8.04, 8.23 and 8.83, showing that all of these compds. strongly inhibit cell growth. Interestingly, each alkylating agent caused significantly different growth inhibition patterns with each cell line. In particular, the correlation coeffs. between the -log GI50 of compd. 1 and its conjugates 2-6 showed extremely low values ($R < 0$). These results suggest that differences in the sequence specificity of DNA alkylation lead to marked differences in biol. activity. Comparison of the correlation coeffs. between compds. 6 and 7, with the same sequence specificity as 6, and MS-247, with sequence specificity different from 6, when used against a panel of 37 human cancer cell lines further confirmed the above hypothesis.

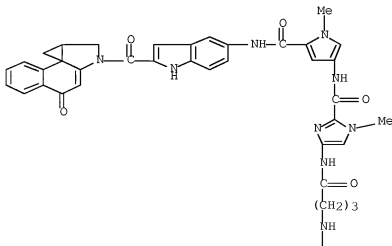
IT 865113-64-0 865113-66-2 865113-67-3
885028-77-3 912572-04-4

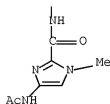
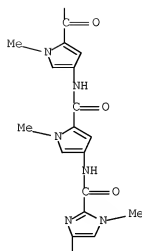
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (antitumor activity of pyrrole-imidazole CBI conjugates with indole linker)

RN 865113-64-0 CAPLUS

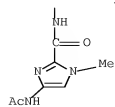
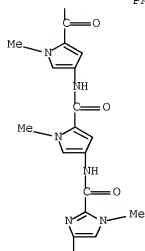
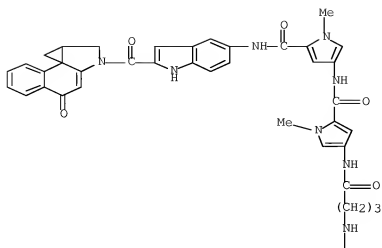
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PAGE 1-A



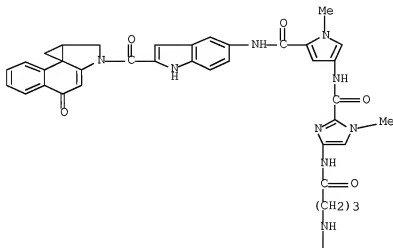


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 methyl-1H-pyrrol-3-yl]amino]-4-oxobutyl]amino]carbonyl]-1-methyl-1H-pyrrol-
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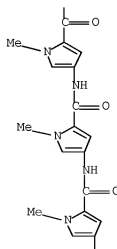


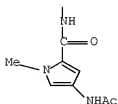
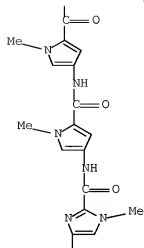
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 pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-
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PAGE 1-A

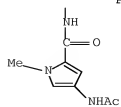
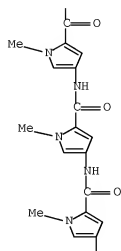
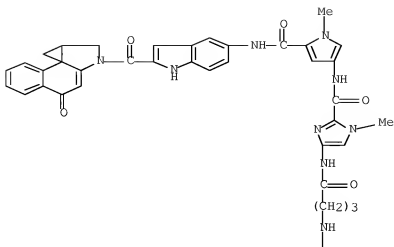


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RN 912572-04-4 CAPLUS
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REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:207991 CAPLUS Full-text
DOCUMENT NUMBER: 144:426676
TITLE: Alkylation of template strand of coding region causes effective gene silencing
AUTHOR(S): Shinohara, Ken-ichi; Sasaki, Shunta; Minoshima, Masafumi; Bando, Toshikazu; Sugiyama, Hiroshi
CORPORATE SOURCE: Department of Chemistry, Graduate School of Science, Kyoto University, Kitashirakawa-Oiwakecho, Sakyo, Kyoto, 606-8502, Japan
SOURCE: Nucleic Acids Research (2006), 34(4), 1189-1195
CODEN: NARHAD; ISSN: 0305-1048
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

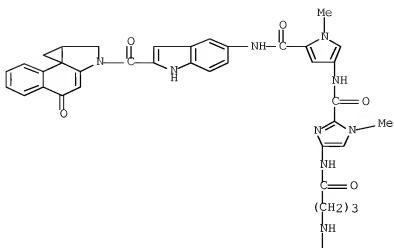
AB We recently developed a new type of pyrrole (Py)-imidazole (Im) polyamide-tetrahydrocyclopropabenzindolone (CBI) conjugate with an indole linker as a stable sequence-specific alkylating agent. In this study, we investigated the gene silencing activities of polyamides A, B and C, which selectively alkylate specific sequences in the promoter region, non-coding strand and coding strand, resp., of the green fluorescent protein (GFP) gene. GFP vectors were transfected into human colon carcinoma cells (HCT116), and the cells were treated with 100 nM of the polyamides for 24 h. Fluorescence microscopy indicated that a significant redn. of GFP fluorescence was only obsd. in the cells that were treated with polyamide C. In clear contrast, polyamides A and B did not show such activity. Moreover, real-time PCR demonstrated selective redn. of the expression of GFP mRNA following treatment with polyamide C. These results suggest that alkylating Py-Im polyamides that target the coding strand represent a novel approach for sequence-specific gene silencing.

IT 865113-64-0 865113-67-3 885028-77-3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(alkylation and gene silencing by; alkylation of template strand of coding region causes effective gene silencing)

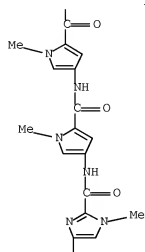
RN 865113-64-0 CAPLUS

CN 1H-Imidazole-2-carboxamide, 4-[[[4-(acetylamino)-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-N-[5-[[[5-[[[4-[[[2-[[[5-[[[2-[[[9,9a-dihydro-4-oxo-1H-benzo[e]cycloprop[c]indol-2(4H)-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]-4-oxobutyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl- (CA INDEX NAME)

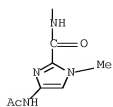
PAGE 1-A



PAGE 2-A

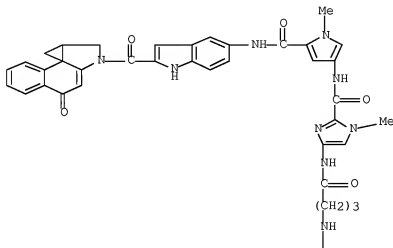


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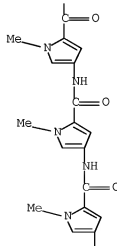


RN 865113-67-3 CAPLUS
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 methyl-1H-pyrrol-3-yl]-1-methyl- (CA INDEX NAME)

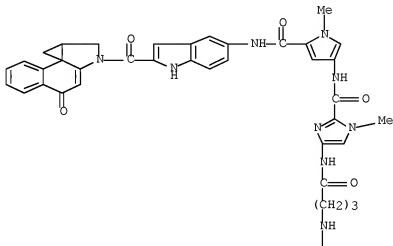
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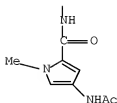
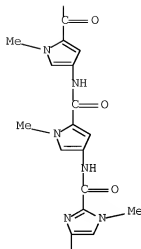


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PAGE 1-A





REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2005:1026947 CAPLUS [Full-text](#)
 DOCUMENT NUMBER: 143:326365
 TITLE: Preparation of indole derivatives for alkylating specific base sequence of DNA
 INVENTOR(S): Sugiyama, Hiroshi; Bando, Toshikazu
 PATENT ASSIGNEE(S): TMRC Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 48 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005087762	A1	20050922	WO 2005-JP4250	20050310
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	GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
	LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
	NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM,
	SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
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AU 2005221959	A1	20050922	AU 2005-221959	20050310
EP 1731519	A1	20061213	EP 2005-720521	20050310

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR

CN 1930151	A	20070314	CN 2005-8007104	20050310
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US 20070191260	A1	20070816	US 2006-598789	20060912
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KR 2007020425	A	20070221	KR 2006-718793	20060913
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IN 2006MN01132	A	20070420	IN 2006-MN1132	20060922
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PRIORITY APPLN. INFO.:			JP 2004-114793	A	20040313
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			WO 2005-JP4250	W	20050310
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OTHER SOURCE(S): MARPAT 143:326365

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

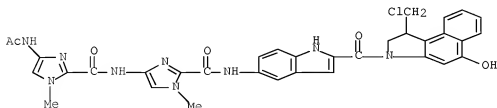
AB Title compds. I [R1 = functional group alkylating DNA;; R2 = H, alkyl, acyl; X = II, etc.] were prepd. For example, EDCI mediated amidation of compd. III [R = 2-carboxyindol-5-ylamino], e.g., prepd. from III [R = OH] in 2 steps, with 1-(chloromethyl)-2,3-dihydro-1H-benz[e]indol-5-ol followed treatment with aq. NaHCO3 afforded compd. IV. In antitumor activity assays for 39 cancer cell lines (in vitro), the av. IC50 value of compd. IV was 100 nM. Compds. I are claimed useful as DNA alkylating agents.

IT 865113-60-6P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of indole derivs. as DNA alkylating agents)

RN 865113-60-6 CAPLUS

CN 1H-Imidazole-2-carboxamide, 4-(acetamino)-N-[2-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]-1-methyl- (CA INDEX NAME)



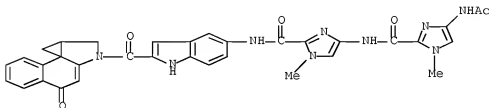
IT 865113-61-7P 865113-64-0P 865113-65-1P
865113-66-2P 865113-67-3P 865113-68-4P
865113-69-5P 865113-70-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(prepn. of indole derivs. as DNA alkylating agents)

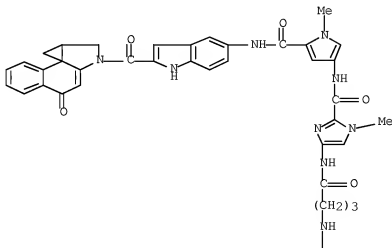
RN 865113-61-7 CAPLUS

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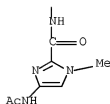
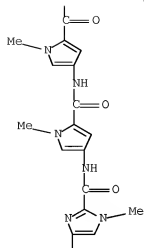


RN 865113-64-0 CAPLUS

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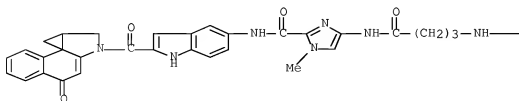


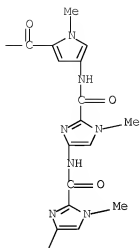
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RN 865113-65-1 CAPLUS

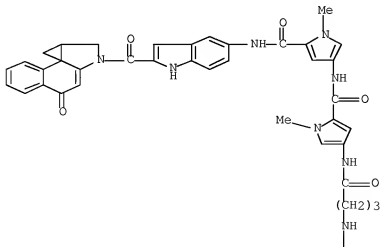
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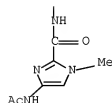
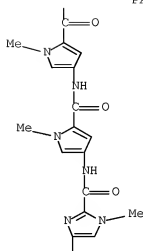




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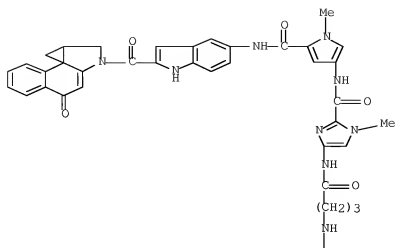
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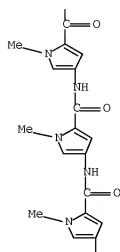


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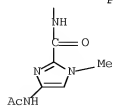
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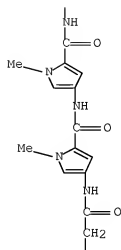
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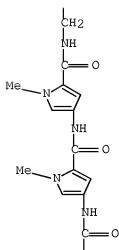
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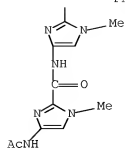


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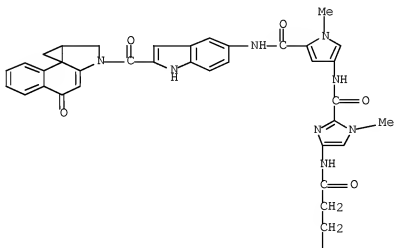


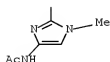
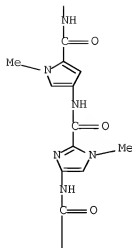
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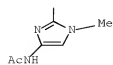
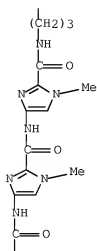
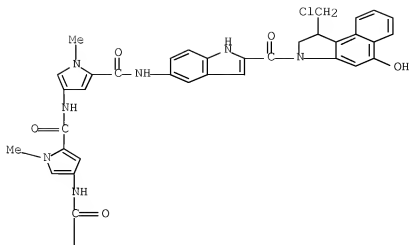


RN 865113-69-5 CAPLUS
 CN 1H-Imidazole-2-carboxamide, 4-[[[4-(acetylamino)-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-N-[5-[[[3-[[[2-[[[5-[[[2-[(9,9a-dihydro-4-oxo-1H-benzo[e]cycloprop[c]indol-2(4H)-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]-3-oxopropyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl- (CA INDEX NAME)





RN 865113-70-8 CAPLUS
 CN 1H-Imidazole-2-carboxamide, 4-[[[4-(acetylamino)-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-N-[2-[[[4-[[[5-[[[2-[[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]-4-oxobutyl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]-1-methyl- (CA INDEX NAME)



IT 865113-72-0

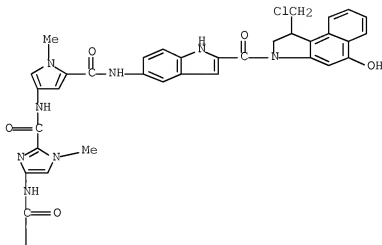
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(prepn. of indole derivs. as DNA alkylating agents)

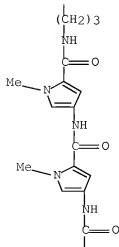
RN 865113-72-0 CAPLUS

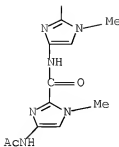
CN 1H-Imidazole-2-carboxamide, 4-[[[4-(acetylamino)-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-N-[5-[[[5-[[[4-[[2-[[[5-[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]-4-oxobutyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl- (CA INDEX NAME)

PAGE 1-A



PAGE 2-A





REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:696700 CAPLUS Full-text

DOCUMENT NUMBER: 139:219341

TITLE: DNA-binding amide-drug conjugates

INVENTOR(S): Szekeley, Zoltan; Hariprakash, Humcha Krishnamurthy; Cholody, Marek W.; Michejda, Christopher J.

PATENT ASSIGNEE(S): The Government of the United States of America,
Represented by the Secretary Department of Health and Human Services, USA

SOURCE: PCT Int. Appl., 50 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003072058	A2	20030904	WO 2003-US6006	20030227
WO 2003072058	A3	20040805		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG			
AU 2003217782	A1	20030909	AU 2003-217782	20030227
US 20050096261	A1	20050505	US 2004-506085	20041001
PRIORITY APPLN. INFO.:			US 2002-361050P	P 20020227
			US 2002-370168P	P 20020405
			WO 2003-US6006	W 20030227

OTHER SOURCE(S): MARPAT 139:219341

AB An amide conjugate comprising a DNA intercalator binds to the minor groove of DNA. A compn. comprising the conjugate and a carrier is useful for treating cancer in a mammal. Thus, 1-(chloromethyl)-5-hydroxy-1,2-dihydro- 3H-

benz[e]indole-8-carboxylic acid (CBIr), a rigid DNA alkylator, was prepd. and conjugated to an imidazole-contg. deriv.

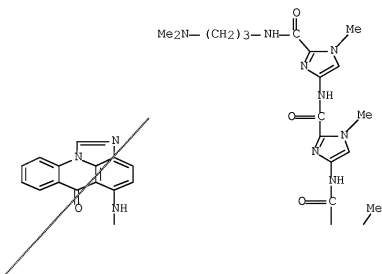
IT 591248-21-4 591248-24-7

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DNA-binding polyamide drug conjugates)

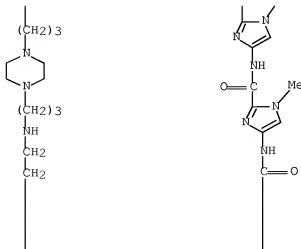
RN 591248-21-4 CAPLUS

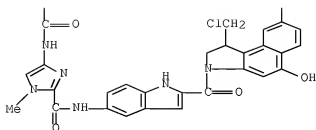
CN 1H-Benz[e]indole-8-carboxamide, 1-(chloromethyl)-N-[2-[[[2-[[[2-[[[3-(dimethylamino)propyl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]-2,3-dihydro-5-hydroxy-3-[[5-[[[1-methyl-4-[[1-oxo-3-[[3-[4-[3-[(6-oxo-6H-imidazo[4,5,1-de]acridin-5-yl)amino]propyl]-1-piperazinyl]propyl]amino]propyl]amino]-1H-imidazol-2-yl]carbonyl]amino]-1H-indol-2-yl]carbonyl]- (CA INDEX NAME)

PAGE 1-A



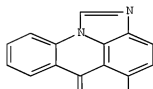
PAGE 2-A

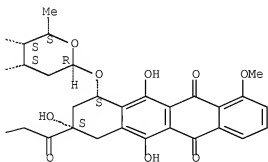
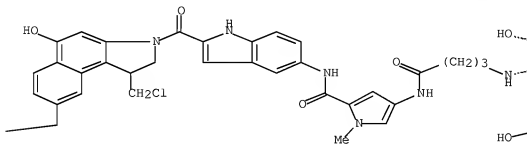
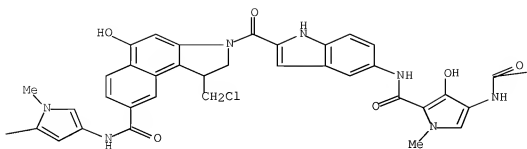


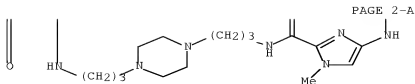


RN 591248-24-7 CAPLUS
 CN 5,12-Naphthacenedione, 10-[[3-[[4-[[5-[[2-[[1-(chloromethyl)-8-[2-[[5-[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-8-[[[1-methyl-5-[[[1-methyl-2-[[[3-[[4-[[3-[[6-oxo-6H-imidazo[4,5,1-de]acridin-5-yl)amino]propyl]-1-piperazinyl]propyl]amino]carbonyl]-1H-imidazol-4-yl]amino]carbonyl]-1H-pyrrol-3-yl]amino]carbonyl]-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-4-hydroxy-1-methyl-1H-pyrrol-3-yl]amino]-2-oxoethyl]-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]-4-oxobutyl]amino]-2,3,6-trideoxy-.alpha.-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



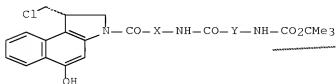




L11 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2003:221652 CAPLUS Full-text
 DOCUMENT NUMBER: 138:255007
 TITLE: Preparation of CBI analogues of CC 1065 and the
 duocarmycins for therapeutic use as anticancer agents
 INVENTOR(S): Boger, Dale L.
 PATENT ASSIGNEE(S): The Scripps Research Institute, USA
 SOURCE: PCT Int. Appl., 35 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003022806	A2	20030320	WO 2002-US28749	20020909
WO 2003022806	A3	20031113		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2459308	A1	20030320	CA 2002-2459308	20020909
AU 2002333548	A1	20030324	AU 2002-333548	20020909
EP 1423110	A2	20040602	EP 2002-798201	20020909
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
JP 2005502703	T	20050127	JP 2003-526882	20020909
US 20050014700	A1	20050120	US 2004-489006	20040827
PRIORITY APPLN. INFO.:			US 2001-318179P	P 20010907
			WO 2002-US28749	W 20020909
OTHER SOURCE(S):	MARPAT	138:255007		

GI



AB 132 CBI analogs I [X, Y = arylene, heteroarylene] of CC 1065 and the duocarmycins having dimeric monocyclic, bicyclic, and tricyclic heteroaroms. substituents were synthesized by a parallel route. The resultant analogs were evaluated with respect to their catalytic and cytotoxic activities. The relative contribution of the various dimeric monocyclic, bicyclic, and tricyclic heteroaroms. substituents within the DNA binding domain were characterized. Several of the resultant CBI analogs of CC 1065 and the duocarmycins were characterized as having enhanced catalytic and cytotoxic activities and were identified as having utility as anti-cancer agents. Thus, I (X = Y = -4-C6H4-) was prepd. starting from 4-H2NC6H4CO2H and the hydrochloride salt of seco-CBI.

IT 372954-19-3P 372954-20-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

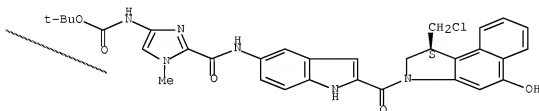
(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

RN 372954-19-3 CAPLUS

CN Carbamic acid, [2-[[[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

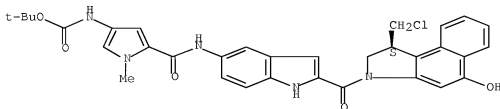
acyl vs.



RN 372954-20-6 CAPLUS

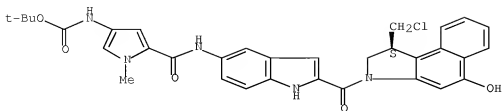
CN Carbamic acid, [5-[[[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CN Carbamic acid, [5-[[[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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Executing the logoff script...

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COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	92.96	520.51
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-12.80	-20.00

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 21:44:28 ON 08 JUL 2008